THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

DECEMBER, 1905.

XANTHELASMA AND CHRONIC JAUNDICE.[1]

By Thomas B. Futcher, M.B. (Tor.),
ASSOCIATE PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD.

(From Prof. Osler's Clinic, Johns Hopkins Hospital.)

Xanthelasma, xanthoma multiplex, or vitiligoidea as an accompaniment of chronic jaundice is a comparatively rare affection. This paper is based on three such cases admitted to Dr. Osler's wards at the Johns Hopkins Hospital. These constitute all the cases that have occurred in the hospital during the first sixteen years ending with May 15, 1905. During this period there had been 18,400 medical admissions, among which there was a large number with chronic icterus. All three cases were admitted between January 30 and June 26, 1901, two having been under observation in the same ward at the same time. The main points in the clinical histories of the cases follow:

Case I. (*Gen. Hosp. No.* 33,689).—*History of typhoid fever; later, cholecystitis; onset of symptoms of gallstones of the common duct two years after the typhoid infection; eight months after the onset of the jaundice the xanthoma plaques made their appearance; xanthomata on gums; exploratory laparotomy; gallstones in the gall-bladder and common duct; spontaneous disappearance of the xanthelasma after leaving the hospital.*

L. J. F., female, white, married, aged thirty-nine years, was admitted to the Johns Hopkins Hospital on January 30, 1901, complaining of "jaundice."

The family history was unimportant, with the exception that her father had had three attacks of jaundice associated with enlarged liver, attributed to the use of alcohol.

[1] Read before the Association of American Physicians, Washington, D. C., May, 1905.

The patient was healthy as a young woman. Married twenty-one years. One child eighteen year ago. Typhoid fever in June, 1897, about three and one-half years before admission. Attack lasted five weeks. After temperature returned to normal, but before she was out of bed, she had a very severe attack of pain in the epigastrium, associated with vomiting. There was great sensitiveness in the upper abdomen, with fever of several days' duration.

The present illness dated from the summer of 1899, two years after the typhoid infection. It began with an attack of abdominal pain, without jaundice. In December, 1899, thirteen months ago, she had several attacks of colicky pain in the epigastrium, after which she became jaundiced. These were accompanied by chills, fever, and sweating. The epigastrium was described as being swollen and very sensitive. From that date there had been repeated attacks of the same character. Jaundice had been persistent, but varying somewhat in intensity. The stools were intermittently clay-colored. Patient lost fifty-three pounds in thirteen months.

The jaundice had existed for thirteen months. There had been severe pruritus. Five or six months ago, and eight months after the onset of the jaundice, she first noticed flat, yellow patches appearing on the palms of the hands, particularly in the folds of skin at the flexures of the joints. Later others appeared in the folds of the elbows, over the olecranon processes, axillæ, sides of the neck, and dorsal surfaces of the toes. At first flat, they subsequently became somewhat raised. The patches over the olecranon processes were sensitive on being struck, and those on the hands were also tender when she used the broom. Friction seemed to favor their occurrence. One particularly thick xanthoma patch developed beneath a ring on the third finger of the left hand. The finger became so sensitive that the ring had to be removed.

Physical Examination. The following were the essential features in the physical examination on admission: Patient still fairly well nourished. Uniformly jaundiced; sclerotics deep yellow in color.

Distribution of Xanthoma Plaques. One very small one on left upper eyelid. Large, flat, yellow patch on right side of neck, 3 x 4 cm. in diameter, with small outlying portions. Similar but still larger one on right side of neck. Smaller one over the fold of left trapezius muscle. *Right arm and hand.* Patch in fold of axilla. Areas of keratosis about elbow and numerous nodular xanthomata around them. Exactly corresponding to the fold of the elbow there was a long linear xanthoma, with small outlying ones. Small patch over one of the creases at the wrist. Two in the palm of the hand over palmar creases. In the creases on the flexor surfaces of all the metacarpo-phalangeal and nearly all the interphalangeal joints there were xanthoma plaques, usually linear, but occasionally irregular in outline. A few patches were scattered over the sides of the fingers and on the knuckles. *Left arm and hand.* The distribution of the

lesions was so nearly identical with those on the right upper extremity that a separate detailed description is unnecessary. A few patches on the upper chest. None on abdomen. Few on dorsal surface of the toes. All the patches had a distinct whitish-yellow tint, differing materially from the color of the jaundiced skin. The majority of the xanthomata were flat and not elevated. A few of the older ones were elevated and slightly nodular, particularly those on the extensor surfaces of the elbows.

The examination of the thoracic organs revealed nothing of importance. The liver was considerably enlarged. The absolute hepatic flatness extended 6.5 cm. below the costal margin in the mammillary line, and 13.5 cm. below the tip of the ensiform in the median line. The gall-bladder was not palpable. The splenic border was rounded and palpable 5.5 cm. from the costal margin.

The stools were light in color, but contained some bile. Urine contained bile pigments. Blood coagulation time on admission was eight minutes and fifteen seconds.

On January 31st Dr. Osler made the following notes: "Interesting points in connection with the case are: (1) sequence of typhoid, cholecystitis, and gallstones; (2) chronic jaundice associated with delayed coagulation time; (3) chronic jaundice associated with the symptom-complex of gallstone in the common duct; (4) xanthelasma.

On February 1st I noted that there was apparently the same sort of lesion on the gums as was found on the extremities. The patches had an opaque yellow appearance and were slightly thickened. The lesion was most evident on the gum over the upper incisors and on that over the lower incisors and canines.

On February 27th a few fresh xanthoma patches were noted for the first time over the patient's back. Under the administration of calcium chloride the coagulation time of the blood became reduced to three minutes and fifty-five seconds.

Operation. On February 28th Dr. Halsted performed an exploratory laparotomy, and found two large stones in the gall-bladder and one in the common bile-duct. There were no indications of xanthomata in the mucous membrane of the gall-bladder or bile-duct.

The patient did well until the eighth day, when she had a severe secondary hemorrhage from the wound. Later she developed a fibrinous pleurisy and a pericarditis, from which she eventually recovered, and was discharged from the hospital much improved, but still somewhat jaundiced, on June 1, 1901.

Dr. Florence Sabin, who was Medical Interne in charge of the patient when she was in the hospital, followed the subsequent progress of the case and she has kindly turned over the notes to me. These may be briefly summarized as follows:

April 7, 1903. General health excellent; still jaundiced. Operation wound healed after eighteen months. Had occasional attacks

of soreness over the liver region, which lasted a few days, during which time the urine becomes very dark.

March 9, 1905. Patient wrote that she was in excellent health and weighed 150 pounds. In reply to a question as to the present condition of the yellow patches she stated that they had entirely disappeared.

In this case the xanthomata were mainly of the flat variety, although there were a few of the nodular variety about the right olecranon. The jaundice had been present for eight months before the onset of the xanthomata. An interesting feature of the case was the spontaneous disappearance of the xanthomata after the patient left the hospital.

CASE II. (*Gen. Hosp. No.* 33,912).—*Gallstones of the common and hepatic ducts and of the gall-bladder; biliary hypertrophic cirrhosis; jaundice of ten years' standing; appearance of xanthomata eight years after the onset of the jaundice. Severe hemorrhages from the nose and uterus; death and autopsy.*

M. A. C., female, white, married, aged thirty-nine years, was admitted to the Johns Hopkins Hospital on February 19, 1901, complaining of hemorrhages.

The family history was unimportant. The patient had always been a healthy woman previous to the onset of the present illness. She was the mother of six children.

The present illness began ten years ago with what she described as "malaria." She had attacks characterized by chills, fever, sweating, and paroxysmal pain in the right hypochondrium at the beginning of the attacks. Jaundice developed at the onset and has since continued with varying degrees of intensity. The attacks of pain, chills, and fever have recurred at intervals up to the present. In March, 1900, she had severe hemorrhages from the nose and uterus, which lasted three weeks. Four days before entrance these recurred and became so severe that she sought admission to the hospital for them. For years "blood blisters" the size of a split pea had appeared over the body, and she was liable to have bruises develop on the slightest injury.

Two years ago, and eight years after the onset of the jaundice, she noticed yellow patches developing on the palms of the hands and subsequently on other parts of the body. There were no symptoms referable to them.

Physical Examination. The following were the essential features in the examination: The patient was fairly nourished. There was intense jaundice and extreme pallor of the skin and mucous membranes. The patient was very freckled. The lungs were clear on percussion and auscultation. The heart showed nothing of importance excepting a faint systolic murmur, probably anæmic in origin, at the mitral area. The relative liver dulness began at the fifth rib in the mammillary line; the absolute at the sixth rib in the same line

not extending quite to the costal margin. Just below the costal margin and inside the mammillary line there was an indefinite rounded mass to be felt, which descended on inspiration and suggested possibly a distended gall-bladder.

Xanthomata. On both of the upper and lower eyelids were long, somewhat raised yellow plaques. In the lines of the palmar surface of both hands and along the sides of the fingers were similar plaques, only less raised. The elbows, both flexor and extensor surfaces, and the axillæ had small rounded tumor-like nodules. Over both buttocks were numerous larger, round, raised, nodular, yellow masses, varying up to 0.5 cm. in diameter. There were a few over the knees and dorsal surfaces of the feet.

There was a spontaneous subcutaneous hemorrhage over the right knee, and a continuous flow of pale bloody fluid from the vagina.

The urine contained abundance of bile pigments, a trace of albumin, but no casts.

On admission the red cells were 1,880,000 per c.mm.; the leukocytes, 15,700 per c.mm.; and the hæmoglobin, 23 per cent. The coagulation time was fourteen minutes. Under complete rest and the administration of iron the patient's condition markedly improved. On March 25th the blood count was as follows: red cells, 4,804,000 per c.mm.; leukocytes, 9700 per c.mm.; hæmoglobin, 58 per cent. Under calcium chloride the coagulation time on this date had become reduced to four minutes and fifty-three seconds. Her condition continued to improve and she progressively gained in weight. She refused an exploratory operation, and, at her own request, was discharged on April 18, 1901.

A few days after her discharge from the hospital the patient died, death having been preceded by severe uterine hemorrhages. Permission was obtained for an autopsy, which was made by Dr. W. G. MacCallum.

Anatomical Diagnosis. Cholelithiasis; obstructive jaundice; biliary hypertrophic cirrhosis of the liver; splenic tumor; acute nephritis; ovarian cystomata; xanthelasma multiplex.

The following were the chief features about the liver and bile passages: The common duct was plugged with a large plum-shaped gallstone. There were several gallstones in the gall-bladder, almost embedded in saccules in the bladder wall. The hepatic duct was filled by a curved cylindrical concretion. Above this the gall-ducts throughout the liver were enormously thickened. The walls of the ducts were almost 0.5 cm. in thickness and of a deep yellow color. On section of the liver the bile-ducts stood out everywhere looking like sclerotic arteries. There were some minute yellow flecks in the mucosa of the walls of the bile-ducts, but there were no lesions typical of xanthomata. The liver was large and measured 35 x 18 x 11 cm., and weighed 2800 grams.

The chief features of interest in this case were: 1. The combination of cholelithiasis, with biliary hypertrophic cirrhosis as a cause of the jaundice. 2. The development of the xanthomata only after the jaundice had existed for eight years. 3. The xanthomata were of two types—flat and nodular.

CASE III. (*Gen. Hosp. No.* 35,296).—*Hypertrophic cirrhosis of the liver; severe uterine hemorrhages; jaundice lasting one and a half years before the onset of the xanthomata; hemorrhages from the gums and uterus.*

L. H., female, white, married, aged forty-two years, was transferred from the surgical to the medical department of the Johns Hopkins Hospital on June 26, 1901, complaining of "liver trouble and jaundice."

With the exception of her father and mother having both died of tuberculosis the family history was unimportant. The patient had had six children and one miscarriage. She had been in the habit of taking an occasional glass of beer or porter for years; no whiskey. For several years she had suffered from attacks of abdominal pain, particularly after indiscretions in eating.

She dated her present illness from five years ago, when she began to have vertigo and general weakness and was forced to give up her work. Her bowels, which had been previously constipated, became rather loose. Two and one-half years ago jaundice developed, which had continued ever since. The stools were gray and the urine high colored. There had been no chills, fever, or attacks of abdominal colic, although she had had indefinite pains in the left hypochondrium. For a year she had noticed a tender spot over the liver, the sensitiveness increasing with pressure or deep inspiration. For the same period she had suffered from repeated attacks of severe uterine hemorrhages. On November 19, 1900, she was admitted to the surgical side of the hospital. She was then jaundiced. The red blood cells were 1,504,000, per c.mm., and the hæmoglobin 28 per cent. The coagulation time was between three and four minutes. Owing to the severe anæmia an exploratory laparotomy seemed inadvisable. Her general blood condition gradually improved, and on May 31, 1901, Dr. Mitchell performed an exploratory laparotomy. Careful examination of the bile passages failed to reveal any gallstones. The liver was much enlarged and presented the appearances of an hypertrophic cirrhosis, which was the surgical diagnosis. The post-operative history was uneventful, and the wound healed well. The jaundice persisted, however, and on June 26, 1901, she was transferred to the medical side of the hospital.

For about one year previous to her admission to the medical ward she had noticed whitish-yellow spots appearing, one below the left eye, the other below the right. These had been gradually increasing in size.

Physical Examination. The patient was of small stature, but was fairly well nourished. Jaundice was intense. The lungs were

normal. Over the apex of the heart was heard a loud blowing systolic murmur, which was transmitted to the axilla, and was also audible over the body of the heart. The liver dulness was considerably increased and extended about 6 cm. below the costal margin in the right mammillary line. The border could not be distinctly felt, owing to the tenderness over the hepatic region. There was considerable tympanic distention of the abdomen; but no ascites. The spleen was not palpable.

Situation of the Xanthomata. Over the lower right eyelid there was a flat yellow xanthoma patch measuring 1 cm. x 2 mm. Above and within the left internal canthus there was a similar one measuring 1.5 cm. in diameter. Careful search failed to reveal any xanthomata on any part of the body.

The urine contained abundance of bile pigments, but no albumin or casts were present.

During her stay on the medical side she had some bleeding from the lips and mucous membrane of the mouth. On July 4, 1901, she was discharged from the hospital at her own request.

The patient returned to the hospital for observation on November 28, 1904. The jaundice was still present. She had had some bleeding from the gums and from a scratch on the ear. The liver border was palpable three fingers' breadth from the costal margin.

In this case the xanthomata were confined to the eyelids. The patient gave a definite account of their appearing one and a half years after the onset of the jaundice. The case was therefore not one in which a patient with xanthomata of the lids developed a chronic jaundice, but the reverse. Although the xanthomata were not so widely distributed as in the previous cases, yet there was no reason to doubt that they were dependent on the hepatic disease or the jaundice.

Xanthelasma is not a common disease under any circumstances. The cases in which it is limited to the eyelids (*xanthoma palpebrarum*) occur much more frequently than those where the lesions are more generally distributed (*xanthoma multiplex*). The majority of the latter form are of congenital origin in the young, or associated with jaundice or glycosuria in adults.

Xanthomata occur in two forms, either as flat plates or plaques (*xanthoma planum*), or as nodules or tumors (*xanthoma tuberculatum* or *tuberosum*). According to Crocker they represent little more than differences in position, shape, and degree of development.

Xanthoma palpebrarum constitutes the bulk of the cases, and the lesion here is in the form of *plaques*. It commences most frequently on the left upper eyelid near the inner canthus, and may form a semicircle of the whole eye. Later the right side becomes affected and the lesion is usually symmetrical. The patches have a chamois-leather yellow color. They are either not at all or only slightly raised

and are situated in the corium. They are soft and smooth and the skin does not seem thickened when it is picked up.

Xanthomata when of the *nodular* variety have the same color as the plaques, but project more or less above the surface. They vary in size from a millet-seed to a large pea, and in rare instances may be 2 or 3 cm. in diameter. The small ones are convex, round or oval, and often have a fine network of capillaries over them. They are soft and smooth to the touch. The larger ones are made of conglomerations of the smaller ones, and are irregular in contour and are more or less firm in consistence, depending upon the amount of connective tissue they contain.

Xanthoma multiplex in the adult is most frequently associated with jaundice of long standing, and it is this form with which we are especially interested in this paper. The first reference I have been able to find of the association of xanthelasma with chronic jaundice is in a paper by Thomas Addison and William Gull,[1] published in 1851, and entitled "On a Certain Affection of the Skin, Vitiligoidea—α, Plana, β, Tuberosa. With Remarks and Plates." They report five cases of a skin affection with which they were not familiar, and, owing to a certain resemblance between it and the disease described by Willan as vitiligo, they suggested the name *vitiligoidea*. They distinguished two varieties of the affection: the flat, to which they gave the name *vitiligoidea plana*, and the nodular, which they designated by the name *vitiligoidea tuberosa*. Of the five cases three were in patients with chronic jaundice. In one of the three the lesions were distributed in the creases of the wrists, hands, and interphalangeal joints, similar to the distribution in Cases I. and II.

The lesions of xanthoma multiplex in chronic jaundice are both in plaques and nodules, the former type prevailing. They may involve the skin, mucous and serous membranes, and the tendons. The commonest positions are the eyelids, where it is said to most often begin, the palms and soles and backs of the hands and feet, flexures of the wrists, and the buttocks in and near the cleft and about the anus. It is of interest to note that in Cases I. and II. the xanthomata made their appearance first on the palms of the hands. The plaques are most commonly found on the eyelids, joint flexures, and mucous membranes. In Case I. the gums were affected. In Case II. there were suggestive indications of xanthomata in the mucous membrane of the bile-ducts on macroscopic examination, a suspicion which was confirmed on microscopic study of the sections. The nodules usually occur on the extensor aspects of the joints, particularly on parts exposed to irritation, as the knuckles, elbows, and knees. In xanthoma multiplex symmetrical arrangement of the lesions is the rule, and is often very striking. This was a marked

[1] Guy's Hospital Reports, new series, 1851, vol. vii. p. 265.

feature of Cases I. and II., and was also true in Case III., in which the lesions were limited to the eyelids. The xanthomata appear gradually and are slow in their development. After months or years their growth ceases, and there is usually no future change in them. Crocker states that three instances have been reported in which spontaneous disappearance occurred after several years. In Case I. the xanthomata had entirely disappeared within four years after the patient left the hospital, and about four and a half years after their first appearance.

The xanthomata rarely cause any inconvenience excepting from their disfigurement. Occasionally, burning, prickling, or itching have been experienced, and when they have occurred on the palms of the hands or knees, grasping objects or kneeling may cause some discomfort, or even pain.

In 1882 a committee composed of Jonathan Hutchinson, Alfred Sangster, and H. Radcliffe Crocker[1] was appointed by the London Pathological Society to report on 2 cases of xanthoma multiplex, one of which was demonstrated before the Society by Stephen Mackenzie, and the other by James Startin. They collected data of 23 cases of xanthoma multiplex in adults with jaundice; 10 of these were in males, 12 in females, and in 1 the sex was not stated. It would seem, therefore, that women are a trifle more liable to the affection than men. They also found records of 5 cases of xanthoma multiplex in adults without jaundice; 4 of these were males and 1 a female. Statistics of 8 cases of xanthoma multiplex, either congenital or commencing before puberty, were also collected from the literature. It was not possible to definitely ascertain the sex in these cases, but 4 were believed to be males and 4 females.

Some of the conclusions of this committee regarding xanthoma multiplex were as follows: 1. That cases occurring before puberty, although structurally the same as those beginning at a later period, are etiologically different, have no traceable connection with hepatic disease, but are probably to some extent hereditary. That they may be congenital, and that the eyelids always escape. 2. That four-fifths of the cases of xanthoma commencing after puberty are associated with chronic jaundice from obstruction of the bile-ducts. That in some of the others the health has been perfect, but that diabetes has been observed more than once. That the eyelids are almost always involved and almost invariably the starting point. Occasionally spontaneous involution occurs. That, as regards sexes, the numbers affected are nearly equal.

From the standpoint of *etiology* there seems little doubt but that the jaundice is the exciting agent in the xanthoma multiplex cases accompanied by this symptom. The hepatic conditions causing the

[1] Transactions of the Pathological Society of London, 1882, vol. xxxiii. p. 376.

jaundice have been found to be cholelithiasis, stricture of the bile-ducts, atrophic and hypertrophic cirrhosis of the liver, hydatids, and cancer. How the jaundice acts in effecting the changes in the corium is not known, but presumably it is through the agent of a toxin. Besnier, Hollopeau, and Kaposi regard the jaundice and liver troubles as secondary, and due to the development of the xanthomata in the viscera. Crocker states that the order of development of the clinical features does not support this view. It may be of interest here to note that Besnier and Gailleton have described a condition in hepatic affections which they call *xanthochromia* of the skin, and not due to jaundice in some cases. It is more marked on the face and trunk than on the extremities, the conjunctiva and buccal mucous membrane are uncolored, and there is no bile in the urine and feces.

There is considerable difference of opinion as to the *pathology* of this skin affection. Xanthomata were excised from Cases I. and II., and the sections were carefully studied by Dr. W. W. Williams, of the Harvard Medical School, whose report has not yet appeared, but who has kindly furnished me with a copy of his histological examination. In association with these cases, sections from a xanthoma palpebrarum complicating a case of diabetes insipidus, admitted to the Johns Hopkins Hospital and reported by me before this Association last year, were also studied. The findings in all three cases were practically identical, and I quote briefly the main features of Dr. Williams' report:

"The epidermis is essentially normal, although in places there are large vacuolated cells in the lower part. Below this is a layer of practically normal connective tissue, which, however, contains a few pigmented spindle-shaped cells. Branching off from this layer are numerous larger and smaller fibrous bands, becoming continuous with the normal tissue deeper down, and forming an irregular network. These trabeculæ are composed of fibrous connective tissue, with a few deeply staining, long, narrow nuclei and some delicate elastic fibres. Also a few delicate pigment granules are to be seen.

"Within the meshes of this fibrous reticulum are masses of pale cells, although in places the same pale cells occur singly or in pairs between the connective-tissue fibres. Surrounding each cell in these groups is a delicate reticulum containing here and there fine elastic fibres.

"These pale cells (so-called xanthoma cells) vary much in size; and though some are small and mononuclear and others large and multinuclear, they are all otherwise similar. There is no definite cell membrane, and the protoplasm is everywhere finely granular and contains more or less refractive granules, which react to the fat stains. Some of the cells are vacuolated, and others definitely phagocytic.

"The nuclei are, as a rule, oval, with a distinct membrane, vesicular, and often contain several nucleoli. They are usually more or less centrally situated. Mitosis is seen in some of these pale granular cells. The number of nuclei vary from one to twenty.

"About some of the bloodvessels, traversing these groups of cells, slight lymphoid cell infiltration has taken place. The endothelium of some of these vessels and of many lymph spaces is swollen and contains fatty granules. Also in the perivascular lymph spaces are seen pale, granular, vesicularly nucleated cells. In none of the specimens were any polymorphonuclear leukocytes, nerves, or muscle cells found, or any involvement of the hair follicles or sebaceous or sweat glands noticed."

Dr. Williams' report on the histological examination of the bile-ducts in Case II., which came to autopsy, is exceedingly interesting. "The walls of the bile-ducts are considerably hypertrophied, containing many elastic fibres, and the lumena are lined with a mass of lymphoid and plasma cells, and also many large, pale, granular, vesicularly nucleated cells, similar to those already described in the skin lesions." Apparently these changes were regarded as due to the development of xanthomata in the bile-ducts.

In a communication from Dr. Williams he wrote: "In my conclusions on these growths I maintained that they were of endothelial origin, though many described in the literature, and also one I described as really lipomata—lipoma xanthomatodes."

The description given by Crocker[1] and Touton for sections of xanthoma palpebrarum agree closely with Williams' report. There is no essential difference between the plaques and the nodular variety. In the latter the bulk of the lesion is more superficial, and is in the papillary layer pushing up the epidermis above the level of the surrounding surfaces. The connective tissue is much more abundant than in the case of the plaques, and is most marked about the hair follicles and sebaceous glands. The fatty masses are less conspicuous and yellow oil globules infiltrate the meshes between the fibrous tissue. Crocker holds that in the development of the xanthomata inflammation is the primary factor; that the xanthoma cells and the connective-tissue growth are secondary, and that the whole process is of toxæmic origin.

Köbner thinks that the lesions are derived from embryonic remnants. Török claims that the xanthoma plaque is composed of adipose cells interrupted in their progress to complete evolution, and that it is not a tumor, but an excess of growth. Unna holds that the fat in xanthoma palpebrarum is a sort of fatty infiltration of the orbicularis muscle, the fat being in the lymph spaces and the giant cells being sections of dilated lymphatics. Pollitzer claims that the eyelid lesion is the product of the degeneration of embry-

[1] Diseases of the Skin, third edition, p. 745.

onically displaced muscle fibres. This view has not been supported and seems to be disproven by the clinical fact that in both children and adults, after the lesion begins on the eyelids, it subsequently makes its appearance on various parts of the body.

There is no special difficulty in making a *diagnosis*. About the only condition likely to be confused with it is *milium palpebrarum*. These are usually small and situated near the inner canthus of the upper lid. Being due to retained sebaceous secretion, they are generally white, and occasionally the dark-colored opening of the duct may be seen. Milium is more superficial and firmer, and the contents of the nodule can easily be peeled out. Politzer refers to cases of *multiple dermoid cysts* of the skin, in which the diagnosis was possible only on microscopic examination of excised tissue.

After developing gradually for years the xanthomata become stationary and persist in the majority of cases throughout life. In rare instances, as in Case I., spontaneous involution may occur. In this case operation had been performed with a relief of the gallstone symptoms and almost complete disappearance of the jaundice.

There is practically no treatment for the condition, excepting incision, that yields results. It seems almost certain that the xanthomata are due to the jaundice or to some associated toxic substance circulating in the blood. Consequently efforts should be made to relieve the causes of the jaundice, which is possible at least in the cases of cholelithiasis.

SUMMARY. The three cases here reported were all in women, their respective ages being thirty-nine, thirty-nine, and forty-two years. The duration of the jaundice before the xanthomata appeared was eight months, eight years, and one and one-half years. The cause of the jaundice was gallstones of the common duct in two cases, one of which also had biliary hypertrophic cirrhosis of the liver, and in the third case hypertrophic cirrhosis of the liver alone. In all three cases the eyelids were involved, in one these only. In the other two there were lesions on the extremities and to a less degree on the trunk. In two cases the xanthomata appeared on the hands first; in the third on the eyelids. The xanthomata were chiefly in the form of plaques in all the cases. There were a few nodular xanthomata in Cases I. and II. The distribution was strikingly symmetrical. In Case I. there were xanthomata on the gums, and in Case II. histological examination of the bile-ducts showed that xanthomata of the mucous membranes of the ducts were present. At all events, the histological picture showed cells identical with the "xanthoma cells" of the lesions in the skin. In Case I. there was a spontaneous disappearance of the xanthomata four and one-half years after their onset, and about four years after the gallstones were removed at operation. Two of the cases were operated on, and one came to autopsy, so that the causes of the jaundice were definitely ascertained.

Four-fifths of the cases of xanthoma multiplex in adults occur in chronic jaundice. In these cases men and women are about equally affected, with possibly a slightly greater frequency in the latter. The hepatic conditions causing the jaundice have been found to be gallstones, stricture of the bile-ducts, atrophic and hypertrophic cirrhosis of the liver, hydatids, and cancer. In addition to the skin, the tendons and mucous membranes may occasionally be involved. The onset is said to be most frequently on the eyelids. The xanthomata accompanying jaundice are believed to be directly traceable to the latter or to some associated toxic substance circulating in the blood. Symmetry in distribution is often striking, and the tendency to develop in the folds and creases of the joints is a remarkable feature. The views as to the actual nature and sequence of tissue changes in the lesions vary much. Crocker thinks that inflammation is the primary factor and that the xanthoma cells and connective-tissue growth are secondary, and that the whole process is of toxæmic origin. Williams' careful histological study indicates strongly that the xanthomata are of endothelial origin. Once they develop they rarely disappear. Spontaneous involution is rare. No treatment other than surgical in suitable cases is of any avail. The indications are to relieve the underlying process if possible.

THE NATURE AND THE LESIONS OF CIRRHOSIS OF THE LIVER, WITH SPECIAL REFERENCE TO THE REGENERATION AND REARRANGEMENT OF THE LIVER PARENCHYMA.[1]

By A. O. J. Kelly, M.D.,

ASSOCIATE IN MEDICINE, UNIVERSITY OF PENNSYLVANIA; ASSISTANT PHYSICIAN TO THE UNIVERSITY HOSPITAL; PROFESSOR OF THE THEORY AND PRACTICE OF MEDICINE, UNIVERSITY OF VERMONT; PATHOLOGIST TO THE GERMAN HOSPITAL, AND PHYSICIAN TO ST. AGNES' HOSPITAL, PHILADELPHIA.

The study of cirrhosis of the liver has been approached from several points of view—etiological, anatomical, and clinical; but since the disorder was first described by Vesalius special interest has centred in the obvious and most conspicuous feature of the lesions—the fibrosis; so much so, indeed, that the term "cirrhosis," first employed by Laennec to describe the yellowish (κιρρός) "hobnails," which he regarded as new-growth, has by a curious transference of meaning become almost inseparable from, with some writers practically identical with, the sclerotic process; and, indeed,

[1] Read before the Association of American Physicians, Washington, D. C., May, 1905.

by the ill-informed its meaning is not infrequently expanded so as to include sclerotic and fibrotic processes in other organs. As contrasted with the conspicuous fibrosis, the changes in the parenchyma of the liver in cirrhosis have received comparatively scant attention; they are commonly, though of course not universally, looked upon as progressively and continuously degenerative or atrophic, usually subsidiary in importance, and secondary to, consequent upon, the changes in the interstitial tissue. It is true, however, that the so-called pseudobile-ducts or canaliculi, present in many cases of cirrhosis, are usually nowadays looked upon as evidences of a regenerative process; that the liver cells are further capable of quite extraordinary regeneration is now well known in consequence of experimental investigations and the study of the changes following acute yellow atrophy and allied processes, and such regeneration is generally recognized in the adenoma-like formations that occur under diverse circumstances; but that any noteworthy regeneration of the liver cells is a part of ordinary cirrhosis is not commonly taught.

It has long been recognized, however, that much as we have felt that we know concerning the liver and its perversions of function and alterations of structure, much more remains to be learned; though the clinical recognition of cirrhosis of the liver may be a comparatively easy matter in many cases, the condition is not infrequently overlooked, and it constitutes a not uncommon accidental finding at the necropsy; and the divers classifications of the process (or processes) proposed by different writers—some based largely, others exclusively, upon the nature, disposition, arrangement, etc., of the fibrous tissue—and the discussion relative to what is and what is not cirrhosis (in an acceptable sense) indicate only too well that many questions pertaining to the subject still await solution. The general obscurity of many of these questions was well emphasized by Dr. Cheadle[1] in his Lumleian lectures for 1900, when he suggested the following as "among the questions awaiting an accepted and final settlement: Is atrophic cirrhosis—that is, the contracted hobnail liver—always of alcoholic origin? Is the liver small from the first, or is there an earlier stage in which it is enlarged, becoming contracted later; or is atrophic cirrhosis merely a late stage of hypertrophic cirrhosis; or is there an alcoholic cirrhosis in which the liver is hypertrophied and enlarged from first to last; or is hypertrophic cirrhosis limited to the biliary cirrhosis of Hanot and Charcot of uncertain origin; or, it is even asked, Does the biliary form described by French authorities exist at all as a distinct entity? Again, is ascites limited to the atrophic form, almost unknown in the hypertrophic; while, on the other hand, is jaundice rare in atrophic cirrhosis, almost invariable in the hypertrophic

[1] Some Cirrhoses of the Liver, 1900.

form? Are the microscopic characters of monolobular cirrhosis, with hyperplasia of the bile-ducts, as described in the biliary cirrhosis of Hanot and Charcot, found only in cases that correspond to that clinical type; or are they met with in both atrophic and hypertrophic cirrhosis of alcoholic origin? The part played by alcohol, syphilis, and malaria in causation and their connection with special types of the affection; the incidence and significance of perihepatitis; the curability of ascites; the efficacy of paracentesis or its uselessness in the treatment of it; the possibility not of curing cirrhosis, but of prolonging the life of the cirrhotic patient by this or other means; the conditions under which the course of cirrhosis can be favorably influenced in this way, are other points about which there is a lack of general agreement."

Although progress has been made since the time of Dr. Cheadle's lectures, which was about contemporaneous with a renewed interest in cirrhosis of the liver, much still awaits elucidation. The difficulty in the past has been due largely to the points of view from which the phenomena of cirrhosis have been studied, to the fact that the late lesions are those that necessarily have been most investigated, to the bases of classifications commonly adopted, and to the comparative inelasticity of the descriptive terms employed, all of which are excellently intimated by Dr. Cheadle in his queries. The recent studies and several communications of Kretz,[1] however, throw considerable light upon the nature of cirrhosis; and the still more recent communications by MacCallum[2] and Böstrom,[3] as well as the results of some experimental work, notably recently by Pearce,[4] lend confirmation to his views. My own work, which in some particulars is merely confirmatory of the already published work of Kretz and of MacCallum, is based upon a study of the thirty cases of cirrhosis and of many other cases of disease of the liver, that have come to necropsy at the German Hospital, Philadelphia, during the last eight years; certain clinical data of patients treated in the German Hospital during the last fifteen years, in whom a diagnosis of cirrhosis of the liver was made—for permission to use which I am much indebted to Dr. James C. Wilson, physician-in-chief to the German Hospital; several cases of cirrhosis observed on Dr. Musser's service in the University Hospital, for permission to utilize which I am much indebted to Dr. Musser; several cases observed on my own service at St. Agnes' Hospital; many of Professor Kretz's

[1] Ueber Lebercirrhose, Wien. klin. Woch., 1900, Bd. xiii. p. 271; Lubarsch und Ostertag's Ergebnisse der allg. Path. und path. Anat., 1904, Bd. viii. p. 473 (bericht über das Jahr., 1902); Verhandl. der Deut. path. Gesellschaft, 1904, Bd. viii. p. 54; International Clinics, 1905, 15th series, vol. iii. p. 289.

[2] Regenerative Changes in Cirrhosis of the Liver, Journal of the American Medical Association, 1904, vol. xliii. p. 649.

[3] Lebercirrhose, Deut. med. Woch., 1905, Bd. xxxi. p. 167.

[4] A paper on Experimental Cirrhosis of the Liver, read at the meeting of the American Association of Pathologists and Bacteriologists, in Chicago, April, 1905, and to be published in the Journal of Experimental Medicine.

preparations; and other pieces of tissue from unusual cases, for which I am indebted to several friends, notably Dr. W. F. Hamilton, of Montreal; Dr. Allen J. Smith, of Philadelphia; Dr. W. M. L. Coplin, of Philadelphia (spontaneous cirrhosis in dogs), etc. I shall consider (1) the structure of the liver in so far as it has a bearing upon the changes in cirrhosis; (2) the changes in the parenchyma of the liver in cirrhosis; (3) the changes in the connective tissue in cirrhosis; and (4) the permissible deductions with regard to the nature of cirrhosis that may be drawn from the foregoing.

THE STRUCTURE OF THE NORMAL LIVER. Although it is largely supererogatory at this day to discuss the structure of the normal liver, a clear conception of the cirrhotic process is best attained by bearing in mind that, as recognized years ago by Hyrtl[1] and recently especially emphasized by Kretz, the liver is not made up of acini in an acceptable sense. While the physiological unit of the liver is that collection of cells drained by a radicle of the bile-duct, this unit is scarcely delimitable anatomically, although Sabourin[2] has made an attempt to do so; nor are the so-called acini, or lobules, cross-sections of which, surrounded by connective tissues, form such a conspicuous feature of microscopic sections, of such simple structure as at first sight appears. Study of the liver in serial sections and its reconstruction show that the liver parenchyma does not form isolated acini, or lobules, everywhere surrounded by connective tissue, but that what appear to be acini are merely cross-sections of liver cells arranged as a mantle about the numerous dendritic ramifications of the hepatic vein, and that this mantle is nowhere discontinuous, forming, on the contrary, a continuous whole, everywhere connected, particularly at the points of junction of the sublobular, lobular, and lobar veins. The intimate relationship that the liver cells structurally bear to the hepatic vein is further shown by the radial disposition of the cells about the branches of this vein—the so-called central veins. Toward the periphery of the liver anastomoses may sometimes be found between branches of the hepatic vein, and in some of the lobules one sometimes encounters rather large branches of the central vein, about which the liver cells are arranged radially. Thus we find that the liver consists not of acini, but of mantles of cells arranged radially about the arborescent ramifications of the hepatic vein, and that cross-sections of so-called acini are really cross-sections of cell mantles, which, however, may also be cut longitudinally or tangentially.

Sabourin has attempted to modify the current conception of the so-called acini in that he looks upon the centre of the acinus, or lobule (according to his conception), as the portobiliary nodule, the point of breaking up of a radicle of the portal vein, and of the

[1] Lehrbuch der Anatomie des Menschen, 1873, 12te Aufl., p. 639.

[2] Étude comparé du foie de l'homme et du foie du cochon, Revue de méd., 1901, tome xxi. p. 384.

confluence of the biliary capillaries to form a biliary radicle; the extent of the acinus, as the area of distribution of a portal radicle, with its accompanying hepatic artery, bile-duct, and related liver cells; and the periphery of the acinus, as the so-called rectilinear veins, small intralobular veins, formed by fusion of capillaries, that empty at right angles into the central veins. In the swine these rectilinear veins are accompanied by connective tissue from the periportal connective tissue to the central veins, and Sabourin believes that the counterpart of this exists in the human subject; it is to be found especially in cases of long standing chronic congestion. This conception of the architecture of the liver is of some interest, since it serves to correlate the anatomical with the physiological unit; but as far as we are concerned at present, it merely substitutes the portal for the hepatic vein, since in both cases the hepatic cells form a continuous mantle—of the branches of the portal vein in the one case, of the branches of the hepatic vein in the other case.

Pervading and filling the spaces left between the arborescent ramifications of the hepatic vein with its cell mantles are the radicles of the portal vein, accompanied by the hepatic artery and the bile-ducts, all supported by connective tissue (the capsule of Glisson), sparse in some places, more abundant in others. But such is the arrangement of the intertwinings of the "portal tree" and the "hepatic tree," that the finest ramifications of the one are everywhere separated from those of the other by a collection (mantle) of liver cells.

As distinguished from most other organs, the liver has two sources of blood supply—the portal vein and the hepatic artery—which commingling form a plexiform capillary network, in the meshes of which the liver cells are arranged. Ultimately, the capillaries unite again to form the radicles of the hepatic vein—the rectilinear veins of Sabourin which empty into the so-called central veins. The circulation within the liver, which is not only interesting in itself, but of much importance in connection with certain features of cirrhosis, has recently been studied attentively by Opie.[1] It has long been known, and Opie directs renewed attention to the fact that one of the important characteristics of the liver is its susceptibility to variations in blood pressure, saying: "The portal vein, hepatic artery, and hepatic vein are in such free communication that the entire lobule can be injected from any one of these vessels. Hence, artificial injections do not define the intralobular distribution of the portal and arterial blood, for doubtless differences of venous and arterial pressure have a part in determining peculiarities of the circulation within the lobule." Opie's experimental studies led him to the conclusion "that both the hepatic artery and portal vein pour their blood into the periphery of the lobule, and here the

[1] Zonal Necrosis of the Liver, Journal of Medical Research, 1904, vol. xii. p. 147.

influence of the arterial blood pressure is most strongly felt. When foreign material reaches the liver by the portal vein it is washed from the peripheral zone by the arterial blood, and tends to be deposited in a middle zone, where the influence of the opposing circulation is less strongly felt. Hence, it is not improbable that toxic substances capable of causing necrosis of the hepatic cells, brought to the liver by the portal vein, might first exert their effect upon cells within a midlobular zone. The periphery of the lobule, moreover, is supplied with arterial blood, and is perhaps for this reason less susceptible to injurious agencies."

CHANGES IN THE PARENCHYMA OF THE LIVER. If we examine attentively the parenchyma of the liver in a moderately advanced or well-advanced case of cirrhosis certain noteworthy deviations from the normal become apparent: (*a*) Changes in the size of the lobules; (*b*) changes in the shape and configuration of the lobules; (*c*) changes in the arrangement of the liver cells; (*d*) degenerative or atrophic and hyperplastic changes in the liver cells; and (*e*) changes in the vascular arrangement and supply.

Changes in the Size of the Lobules. One of the patent and noteworthy features of the lesions of cirrhosis is the marked variation in size of the "granules" or "hobnails," which not only vary considerably in size in different cases, but also in the same case in different parts of the liver, some being notably smaller, others notably larger than the lobules of the normal liver. Long identified as the analogue of the normal liver lobule, it is now well known that many of them are made up of several lobules or of the remains of several lobules; but it is important to bear in mind that some of them are really single lobules, departed, however, somewhat from the normal. The question of the size of these lobules has recently been studied attentively by Kretz, MacCallum, etc. Kretz, pointing out that the normal lobules are roundish-polygonal in shape, with their long axis in the direction of the central vein, states (as is well known) that their greatest diameter is usually a little more than 1.5 mm., and may reach 2.5 mm., whereas the short diameter is about 1 mm., and that in cirrhosis these figures are surpassed, some lobules being much larger, and other collections of cells much smaller. MacCallum found that while the average radius of a lobule (that is, the thickness of the mantle of cells about the central vein) in a number of normal livers is about 0.66 mm., in advanced cirrhosis lobules are encountered that measure from central vein to periphery 1 mm. or more, the small diameter therefore being more than 2 mm. My own observations amply confirm the truth of these statements. I have not, however, been able to confirm Brissaud and Dopter's[1] statement that the lobules of the right lobe are considerably larger than those of the left.

[1] Note sur les differences de volume des lobules hépatiques du foie humain, Gaz. hebd. de méd., 1902, tome xlix. p. 661.

Changes in the Shape of the Lobules. With the central vein as a point of departure, we find that, as already stated, the lobules are roundish-polygonal in shape, their long axis being in the direction of the central vein, and their cross-sections roughly rounded, and that the veins are in reality central—that is, surrounded on all sides by an even thickness or mantle of cells. In diagonal or tangential sections of lobules this is not so apparent, and the picture is altered where several lobules join, or where the liver cells vary somewhat their course to form the continuous mantle, especially about the junctions of sublobular and lobular veins. In cirrhosis there is a notable departure from this shape and configuration; many of the lobules are no longer rounded, but quite irregular in transverse section; many of the cell mantles no longer surround the central veins equally on all sides, but very unequally, so that many central veins are situated eccentrically in a more or less misshapen lobule; many so-called lobules have no central vein at all (and are not tangential sections of otherwise normally arranged lobules); certain lobules (or so-called lobules, usually remains of several) have two, three, four, or more central veins; and often the central vein may be seen in the adjacent interlobular connective tissue. Thus, we ascertain that the mantle of cells covering a central vein varies much in thickness in different regions (transverse planes), sometimes exposing, sometimes covering, the vein to a greater or less extent; and that though isolated collections of liver cells (that is, collections devoid of central veins) do occur, some supposedly isolated collections are merely sections of more or less irregularly proliferating dendritic branches of what may be called the parent stem, or mantle covering a single central vein.

Changes in the Arrangement of the Liver Cells. A conspicuous feature of the normal liver lobule is the radial arrangement of the liver cells about the central vein. In cirrhosis, although this arrangement is preserved to some extent, in many places its partial or complete absence is noteworthy. The architecture of the lobule has become altered so that the cells are arranged irregularly, in parallel rows, etc. This rearrangement of the liver cells is quite as well marked in many of the lobules that have a central vein as in those collections of cells entirely devoid of central veins.

Degenerative or Atrophic and Hyperplastic Changes in the Liver Cells. The degenerative and atrophic changes in the liver cells in cirrhosis—simple atrophy, parenchymatous degeneration, fatty degeneration, fatty infiltration, pigmentary infiltration, etc.—are a part of common knowledge and for a moment need not be further discussed. It is important, however, with a view to the correct interpretation of the lesions, to bear in mind that many cells at the periphery of lobules (or so-called "hobnails") in immediate contiguity to wide bands of connective tissue are by no means atrophic, even in fairly well-advanced cases; on the contrary, it is really note-

worthy that whereas *a priori*, in conformity with prevailing opinions, compression atrophy of these cells should be expected, and is, indeed, often commented upon, the cells that should exhibit this alteration most markedly—that is, those of the periphery of the lobule—often present an unusually plump and healthy appearance, and cannot therefore have been unduly compressed.

Special attention, however, should be directed to the evidences of hyperplasia of the liver cells that are readily found in almost every cirrhotic liver, even in far-advanced cases. Mitoses, it is true, are rarely encountered in advanced cases—largely in consequence of the nature of the process, the advanced stage at which the examination is generally undertaken, and the length of time after death that the liver is obtained, time sufficient for the completion of any mitoses present at death. That many of the liver cells, however, are newly formed is quite apparent from their large, clear, and plump appearance, their rounded (rather than polygonal) outline, the presence of two or more nuclei, and the absence of fat and of pigment from their protoplasm. And what is especially noteworthy is that these cells, sometimes small collections of them, are situated amidst other liver cells normal in size and outline, provided with only a single nucleus each (though sometimes with two nuclei, which is quite normal), and the protoplasm of which is normally pigmented and contains fat. These newly formed cells are usually found at the periphery of a lobule; sometimes they make up a larger or smaller sector of a lobule; sometimes they seem to have compressed the older cells of their immediate vicinity; and sometimes small collections of them are found completely surrounded by wide bands of connective tissue, where, by their generally plump and healthy appearance they convict the connective tissue of exerting less constrictive force than they themselves expansive force. The sector of a lobule sometimes made up of these cells serves, in some cases, to restore more or less completely the normal outline of the lobule—that is, of the mantle of cells covering a central vein—in which event a part of the mantle of cells consists of such newly formed cells arranged irregularly, and a part of older cells arranged radially; in other cases this cellular hyperplasia has occurred in such a manner that the central vein is more or less exposed on one side, and on the other covered with a mantle of cells often twice or thrice the normal thickness.

In acute and subacute, or what may be called recurring, cases mitoses are occasionally encountered (doubtless they would be more frequently encountered were our methods of investigation better thereto adapted), and necrotic and hyperplastic changes may be found side by side in the one lobule.

A characteristic feature of almost all cases of cirrhosis, more conspicuous, however, in some cases than in others, is the bile-ducts or so-called pseudobiliary canaliculi, the nature and origin of which

has for a long time occasioned much discussion. Doubtless the great increase of these structures in cirrhosis, as contrasted with the normal liver, is relative only, and due in part, but only in small part, to mutual approximation of already existing bile-ducts occurring in consequence of loss of the liver tissue; but that most of them are newly formed is generally conceded, and is quite apparent from their excessive number and the evidences of active proliferation (mitosis) that they commonly exhibit. Their origin has not been determined definitely for all cases. Dispensing, for the time being, with a detailed discussion of the question, it seems quite certain that some, at least, of them result from proliferation of previously existing bile-ducts; on the other hand, since they are found in a wide variety of disorders, such as all forms of cirrhosis, acute yellow atrophy, in the neighborhood of hydatid cysts, tubercles, gummas, etc., in other words, in diseases alike only in that they destroy liver tissue; since they differ from normal bile-ducts in the absence or relative paucity of encircling elastic tissue; since they have been found by Ackermann and others to be directly continuous with liver cells; and since in cases in which the liver cells have been much destroyed, they are found in large numbers in what may be interpreted as the remains of the skeleton of the lobule, we are quite warranted in the opinion that they may result from proliferation of the liver cells themselves, constituting in this event a reversion to a less highly specialized type of structure. The important fact only that I wish to point out in this connection is the histogenetic equivalence of the liver cells and the epithelium of the bile-ducts, and the fact that proliferative changes of the liver parenchyma is a conspicuous feature of common cirrhosis.

Changes in the Vascular Arrangement and Supply. Reference has already been made to the fact that the central veins are situated eccentrically in certain more or less distorted and rearranged lobules; that they may be found at the edge of certain lobules or remains of lobules, and even in the interlobular connective tissue, and that certain islets of liver tissue are totally devoid of central veins. Another noteworthy feature is that the central veins appear to have diminished in number in the liver as a whole. Corresponding to the smaller size of many of the cirrhotic livers and the associated loss of the liver parenchyma, the central veins in certain regions sometimes exhibit a mutual approximation, which, however, varies much in different livers and in the same liver in different places. In some regions where considerable hepatic-cell hyperplasia has occurred they are often quite widely separated. But were the central veins not diminished in number in the liver as a whole, we should expect to find, in a small so-called atrophic cirrhotic liver a relative increase in the number of central veins in a given square surface as compared with a square surface of similar size in a normal liver—which, however, is not the case. The absolute lessening of the number of central veins becomes further evident

when we recall the many islets of liver tissue (likely at first sight to be interpreted as more or less distorted lobules) entirely devoid of central veins.

Confirming the view that a number of the central veins have disappeared, we may sometimes find in sections happily cut through the desired plane bulbous and distorted side branches of the sublobular and lobular veins. Furthermore, Kretz, who has studied attentively the circulation in the cirrhotic liver, seems conclusively to have proved, by means of injected and macerated preparations, that the finer ramifications of the hepatic vein are fewer than in the normal liver; that the sublobular and lobular branches are more tortuous and in some places larger and thicker, and that they have attached to them bulbous and distorted side branches, representing, according to him, the atrophic remains of central, sublobular, and lobular veins persisting after the disappearance of the related parenchyma.

Apropos of the circulation in cirrhosis Kretz states: "If in ordinary atrophic cirrhosis an injection is made from the portal vein a small part of the hepatic tissue is, as a rule, so easily permeated that the injection mass passes over into the hepatic vein at a time when a very considerable part of the parenchyma is still uninjected; more particularly after such injection experiments the large turgescent islets of tissue and the small areas devoid of hepatic veins . . . remain unaffected. By injecting the hepatic artery, always decidedly enlarged in these cases, these very areas are most easily injected. They may also be partly injected from the portal vein if an injection mass, which passes with difficulty, is employed. Based upon these observations, the circulation in the diseased liver must be depicted as follows: a small part of the portal blood passes through the remnants of the old acinous channels into the hepatic veins; this passage forms an internal portocaval anastomosis supplementing the external; to the remaining branches of the portal vein more than the normal amount of arterial blood is furnished; this, on the one hand, supplies the granular areas of the parenchyma devoid of hepatic veins, and on the other, the hypertrophic remains of acinous tissue. This excess of blood passes under increased pressure through the remainder of the capillaries, narrowed by atrophy of the acini and lengthened by hypertrophy of the liver tissue. The lengthening and narrowing of the capillary vessels and the excess of arterial blood are the true causes of the increase of portal pressure, as is shown by the occurrence of ascites in subacute atrophy of the liver with regeneration, but without contracting connective tissue."

Miura[1] also has made some interesting observations on the changes in the vascular arrangement that occur in cirrhosis.

[1] Beiträge zur Pathologie der Lebercirrhose, Mittheilungen aus der Medicinischen Facultät der Kaiserlich-Japanischen Universität zu Tokio, 1900, Bd. iv. p. 49.

Pointing out that many of the portal radicles (as is well known) gradually become obliterated, he describes the development, within more or less well-preserved lobules, of communicating vascular twigs directly uniting the portal veins with the central veins. He terms these internal collateral branches, in contradistinction to the external collaterals (those outside of the liver); probably they are not diverse from, or at least originate from, the rectilinear veins of Sabourin. These internal collateral branches, together with their ramifications and the associated portal and central veins, sometimes become provided with connective tissue and serve to subdivide the lobule—in which event the central veins, situated where trabeculæ of such connective tissue join, are likely to be mistaken for portal veins. Usually, however, they may be distinguished by their comparative paucity of elastic tissue, as contrasted with the portal veins. It is scarcely necessary to discuss in detail the well-known changes in the portal vein itself, its increase in thickness and tortuosity, and the obliteration of many of its radicles, especially in advanced cases.

Changes in the Connective Tissue. A study of the connective tissue in almost any well-marked cirrhotic ("coarsely granular") liver shows that it is made up of several sorts of tissue: (1) Some of it is unquestionably newly formed; of this there is no doubt, the debatable point being as to its nature and genesis; (2) some of it is the tissue originally between the lobules—the connective tissue of Glisson's capsule; and (3) some of it is the collapsed and otherwise altered reticulum of certain liver lobules, the cells of which have disappeared, evidently degenerated by some influence and subsequently removed.

As regards the newly formed tissue, its nature and distribution have been studied by a large number of investigators, and little that is new can be added to what is common knowledge. It has been demonstrated by divers methods of investigation, including the use of Weigert's elastica stain, Mallory's connective-tissue and reticulum stain, digestion with pancreatin, etc., that the normal liver contains three kinds of connective tissue: (1) White fibrous tissue, present in the liver capsule and in large amount in the interlobular spaces; (2) elastic tissue, found chiefly about the bloodvessels, to a less extent about the bile-ducts and in the liver capsule, and to a very slight extent in and about the walls of the central veins; and (3) reticulum; according to Mall[1] "a great share of the tissue accompanying the interlobular vessels and all that about the intralobular is reticulated. The peritoneal surface may be viewed as a thickening of the reticulum, intermixed with some white fibres."

Whereas, formerly the fibrosis of cirrhosis was generally thought

[1] Reticulated Tissue and its Relation to the Connective-tissue Fibrils, Johns Hopkins Hospital Reports, 1896, vol. i. p. 171.

to consist almost, if not quite exclusively, of white fibrous tissue, the studies of Hohenemser,[1] Melnikow-Raswedenko,[2] Flexner,[3] McIntyre,[4] Oliver[5] and others have shown us, and anyone can readily demonstrate, that in reality it consists of all the connective tissues of the normal liver—pathologically altered, it is true. The most conspicuous change is the great increase in the elastic tissue—probably more or less intimately related to the great increase in the capillaries derived from arterioles; this elastic tissue not only makes up a large part of the fibrous bands between the lobules, but it is also found to some extent within the lobules, and occasionally a very small amount of it is found about or in the immediate neighborhood of the central veins. A not inconsiderable part of the fibrosis is made up of reticulum—not only the reticulum normally between the lobules, but also the intralobular reticulum—that remaining after the liver cells have degenerated and been removed. This collapsing intralobular reticulum may be quite readily distinguished in tolerably early cases; later, however, when it has become a part of the interlobular fibrosis it can scarcely be recognized as a distinct entity. I believe that Flexner is quite correct in the opinion that the changes in the reticulum in cirrhosis constitute an hypertrophy rather than an hyperplasia of the fibrils.

The distribution of the connective tissue in cirrhosis has long been the subject of much and more or less fruitless discussion; and the many classifications based thereupon have not tended to clarify any of the obscurity connected with the subject. Multilobular, monolobular, and pericellular (as well as certain more or less synonymous terms, such as annular, circumlobular, unilobular, interlobular, extralobular, intralobular, perilobular, intercellular, etc.) are in common use, and are said to be descriptive of special types of the disease. Without entering upon a detailed discussion of the question at the present time, I may point out that while one or the other of these varieties of distribution of connective tissue may appear to predominate in certain cirrhotic livers, all varieties are much more likely to be encountered in the one liver; and while so-called "hypertrophic" or biliary cirrhosis, as contrasted with so-called "atrophic" cirrhosis, is usually characterized by less interlobular fibrosis and an earlier and a finer intralobular fibrosis, it is frequently impossible from a mere microscopic inspection of a section of a cirrhotic liver

[1] Ueber das Vorkommen von elastischen Fasern bei cirrhotischen Processen der Leber und Niere, Virchow's Archiv, 1892, Bd. cxl. p. 192.

[2] Histologische Untersuchungen über das elastische Gewebe in normalen und pathologisch veränderten Organen, Ziegler's Beiträge, 1899, Bd. xxvi. p. 546.

[3] The Nature and Distribution of the New Tissue in Cirrhosis of the Liver, University Medical Magazine, 1900-1901, vol. xiii. p. 613.

[4] Some Points in the Formation of Connective Tissue in the Liver, Glasgow Medical Journal, 1901, vol. lv. pp. 341, 415.

[5] Elastic Tissue in Cirrhosis of the Liver, Transactions of the Chicago Pathological Society, 1901-1903, vol. v. p. 96.

to state to which type of the disease it belongs. Assuredly, in the advanced stages the lesions tend to become very much alike. The difficulty is overcome by some writers who postulate so-called "mixed" cases.

THE NATURE OF CIRRHOSIS. Endeavoring to interpret the foregoing lesions, we find that the most noteworthy feature is the complete rearrangement of the architecture of the liver parenchyma. In consequence of some cause or causes larger or smaller portions of numerous liver lobules have been destroyed, many liver lobules have been destroyed entirely—whence the necrotic changes and the skeleton of the reticulum remaining after removal of the cells that are apparent in the early stages, and the eccentric and otherwise irregular situation of many central veins (the variations in size and outline of the cell mantles) and the complete disappearance of other central veins that are apparent in the advanced stages of the disease. Furthermore, evidences of regeneration and hyperplasia of the liver cells are quite apparent—in the general appearance of many of the cells themselves, in their irregular arrangement, in parallel rows, etc. (as contrasted with the normal radial arrangement), in the large hyperplastic lobular (so-called adenomatous) masses, in the irregular dendritic ramifications of liver cells with a peculiar vascularization and entirely devoid of central veins, in the pseudobiliary canaliculi, etc. Although evidences of secondary atrophy of the liver cells are by no means wanting, especially in advanced cases, the peripheral cells of many of the lobules in early cases, but often also in well-advanced cases, exhibit no evidences of compression atrophy whatever, being plump and well formed and manifesting, therefore, more expansive force than the surrounding connective tissue constricting force; some of the small islets of liver tissue containing central veins, since their peripheral cells exhibit no evidences of compression, must have resulted from degeneration and subsequent regeneration of the liver tissue; and some of the small islets devoid of central veins, since they exhibit no evidence of peripheral compression nor of capillary stasis, cannot have resulted from sequestration of a part of a lobule by invading connective tissue, but must represent regenerated liver tissue. The parenchyma of the liver in cirrhosis, then, consists not only of remnants of the original parenchyma, but also and in large part of regenerated liver tissue that differs from normal liver tissue in that it does not reproduce its typical architecture nor its relation to the bloodvessels—the capillaries and the central veins.

That the liver is capable of this really remarkable regeneration has been amply proved—especially by Ponfick,[1] von Podwyssozki,[2]

[1] Experimentelle Beiträge zur Pathologie der Leber, Virchow's Archiv, 1889, Bd. cxviii p. 209; 1890, Bd. cxix. p. 198; 1895, Bd. cxxxviii. (sup. Heft) p. 81.

[2] Experimentelle Untersuchungen über die Regeneration der Drusengewebe, I. Theil, Leber. gewebe, Ziegler's Beiträge, 1886, Bd. i. p. 259.

von Meister,[1] and others, particularly Pearce[2] recently, who have studied regeneration of the liver experimentally; by Marchand,[3] Meder,[4] Stroebe,[5] Barbacci,[6] Mertens,[7] McCallum,[8] and others who have studied the regenerative lesions following acute yellow atrophy; by the many observers (a good collective list of whom is given by Barbacci), who have studied the adenoma formations in the liver; and by Kretz,[9] Greco,[10] MacCallum,[11] and Böstrom,[12] who have studied the regenerative changes in cirrhosis.

The present is not the time to discuss these regenerative changes in detail, and I must content myself with pointing out that the changes found in cirrhosis when compared with those found, for instance, by Ponfick in experimental hypertrophy of the liver, are found to be identical; that is, for a short time after removal of a portion of the liver mitoses are quite abundant, but later the new-formed liver tissue partakes of the characters of the liver cells in cirrhosis that I have already mentioned—large, clear, plump cells with rounded outlines, containing two or more nuclei, and devoid of fat and pigment, and occurring often in the midst of other cells, differing in no way from the common liver cells (smaller, usually polygonal, with a single nucleus, and normally pigmented and containing fat and sometimes even compressed by the newly formed cells).

The nature of the fibrosis in cirrhosis has long engaged the attention of pathologists; whether it is an inflammatory or a replacement fibrosis is still a matter of discussion. Although the question may not be definitely decided offhand, there are many facts which suggest that the prevailing opinion that the cause of cirrhosis, whatever it may be, engenders a primary overgrowth of connective tissue, is not correct. I have just mentioned certain facts that show that the lesions of the parenchyma in cirrhosis cannot with reason be

[1] Ueber die Regeneration der Leberdrüse nach Entfernung ganzer Lappen, Centralbl. f. allg. Pathologie und path. Anatomie, 1891, Bd. ii. p. 961.

[2] The unpublished paper on Experimental Cirrhosis of the Liver previously referred to.

[3] Ueber Ausgang der acuten Leberatrophie in multiple knotige Hyperplasia, Ziegler's Beiträge, 1895, Bd. xvii. p. 206.

[4] Ueber acute Leberatrophie mit besonderer Berücksichtigung der dabei beobachteten Regenerationserscheinungen, Ziegler's Beiträge, 1895, Bd. xvii. p. 143.

[5] Zur Kenntniss der sogenannten acuten Leberatrophie, Ziegler's Beiträge, 1897, Bd. xxi. p. 379.

[6] Ueber Ausgang der acuten Leberatrophie in multiple knotige Hyperplasia, Ziegler's Beiträge, 1901, Bd. xxx. p. 49.

[7] Lesions anatomiques du foie du lapin au cours de l'intoxication chronique par le chloroform et par l'alcohol, Archives international du pharmacodynamie, tome ii. p. 127 (quoted by Kretz).

[8] Regenerative Changes in the Liver after Acute Yellow Atrophy, Johns Hopkins Hospital Reports, 1903, vol. x. p. 375.

[9] Loc. cit.

[10] Ueber Reproduction der Leber bei Cirrhose, Centralbl. f. allg. Pathologie und path. Anatomie, 1898, Bd. ix. p. 371 (abstracted from La Riforma Medica, 1897, vol. iii.).

[11] Regenerative Changes in Cirrhosis of the Liver, Journal of the American Medical Association, 1904, vol. xliii. p. 649.

[12] Loc. cit.

regarded as secondary to (dependent upon) changes in the connective tissue, since no connective-tissue change with which we are acquainted is capable of causing the noteworthy rearrangement of the architecture of the liver so characteristic of cirrhosis, and, as a matter of fact, the liver parenchyma, even in many advanced cases, exhibits a notable absence of compression atrophy—a change that is so conspicuous, for instance, about a growing metastatic carcinomatous nodule in the liver.

As is well known, there is a disposition among pathologists during recent years to separate from the purely inflammatory conditions certain fibroses, of which the fibroid heart, the chronic granular and arteriosclerotic kidney, certain so-called senile fibroses, sclerosis of the nervous system, and cirrhosis of the liver are conspicuous examples. The scleroses of the nervous system are now almost universally believed to be examples of replacement fibrosis —hypertrophy and hyperplasia of the neuroglia to replace lost or destroyed nervous elements; in the fibroid heart, in many if not all cases, the cardiac muscle has degenerated in consequence of deficient nutritive supply or other cause and becomes replaced by fibroid connective tissue; and other examples of such replacement fibrosis are found in pseudohypertrophic muscular paralysis and the atrophy of certain fetal structures at or shortly after birth. There is considerable evidence that the fibrosis of cirrhosis also is of the same nature, at least in part. The lesions of acute inflammation are scarcely if ever encountered (in view of the chronicity of the process this excites little comment), and when found they are not infrequently due to some complication; the changes in the reticulum are, as suggested by Flexner, hypertrophic rather than hyperplastic, and may be explained by recourse to Ribbert's theory of tissue tension; the new tissue, as a rule, is unusually rich in intercellular substance, as contrasted with cells; and many of the cells are doubtless only evidences of the effort on the part of nature to remove effete matter—necrotic liver cells. On the other hand, we cannot deny that a poison or other etiological factor capable of causing necrosis of the liver cells may also be capable of setting up inflammatory phenomena in the interstitial tissue, although the parenchymatous cells are probably more susceptible to injurious influences, and in other cases the necrotic liver cells, being foreign bodies, act as a source of irritation, whence it is likely that if the fibrosis is largely a replacement fibrosis in some cases, in other cases it is both a replacement and an inflammatory fibrosis.

As regards the nature of cirrhosis, then, I may say with Kretz that it is a chronic focal or localized recrudescing degeneration and partial destruction of the liver parenchyma attended by marked regenerative phenomena on the part of the liver cells leading to complete transformation of the architecture of the liver and followed by fibrosis. It is not a primary interstitial hepatitis, the

changes in the connective tissue being altogether secondary in importance and sequence, probably in large part a replacement fibrosis to fill up potential lacunæ left by degenerated liver cells, and probably in some cases at least partly inflammatory. In consequence of the activity of some poison, or other etiological factor, larger or smaller areas of the liver tissue, that is, of the cell mantles about the central veins, become necrotic and are removed—whereby the central veins become more or less uncovered, thus on cross-section appearing eccentrically situated in more or less misshapen lobules; in some cases in which the destruction of liver cells has been through the entire radius of the cell mantle the central vein may be entirely exposed and may even be found in the interlobular connective tissue, in which event it is very likely to be mistaken for a branch of the portal vein. The cells destroyed are those about the periphery of the lobules—in the area of portal distribution, conforming to the fact that the etiological factor (poison) is usually carried by the portal vein. In case the poison is carried by the hepatic artery (as seems likely in some general infections) the lesions may be somewhat diverse, in the beginning of the process at least, and it is by no means improbable (though this still awaits proof) that the differences between the common or Laënnec's cirrhosis and so-called hypertrophic cirrhosis are in part at least dependent upon the source (portal vein or hepatic artery), in part also upon the nature, of the provoking cause. Following the primary destruction of certain liver cells, the intact cells, exhibiting a remarkable regenerative capacity, attempt to replace the lost cells and sometimes succeed in restoring more or less completely the volume of the cell mantles. The cells that regenerate are those in the immediate vicinity of those that have become necrotic, that is, in the ordinary case in which the destruction is not widespread, cells toward or at the periphery of the lobule—which thus are not only most exposed to the deleterious influence of poisons carried by the circulation, but in consequence of being better supplied by arterial blood are also better adapted for repair. I am rather inclined to believe, in view of Opie's researches on the circulation within the lobules, that the primary destructive action may be exerted, at least sometimes, in the so-called midlobular zone—at all events, not immediately at the periphery; that the peripheral cells, being better supplied with arterial blood, survive when others nearer the centre of the lobule succumb, and that these peripheral cells also serve as a focus of regeneration, though, of course, the cells nearer the centre of the lobule also regenerate. I am somewhat confirmed in this opinion by the characteristics and disposition of many of the pseudobiliary canaliculi, which are often most numerous in the skeleton of those lobules that have been much destroyed, and seemingly grow from the periphery into the lobule, in a manner quite analogous to Ponfick's and others' descriptions of their growth into granulation tissue after destruction

of the liver cells. As is now generally conceded, these pseudobiliary canaliculi sometimes grow from pre-existing bile-ducts, but as I have already pointed out, and as is well known, they also develop from liver cells, which in this respect are histogenetically equivalent with the epithelium of the bile-ducts. It is also not unlikely that some of the surviving peripheral cells by proliferation give rise to certain of the hyperplastic islets of liver tissue devoid of central veins.

The continuing activity of the etiological factor leads to a continuous or recrudescing death of certain old as well as newly formed liver cells, which in turn is followed by renewed regeneration. This continuous degeneration and regeneration ultimately lead to complete transformation of the architecture of the liver; certain lobules are entirely destroyed, others are partly or completely rearranged, some are markedly hyperplastic though tolerably well arranged, some show dendritic and other irregular proliferation, new islets of liver tissue entirely devoid of central veins appear, and what is especially important, new circulatory conditions—capillary and venous—arise.

Concurrent with the degeneration of the liver cells, the framework of the lobules collapses and participates in the formation of the fibrosis. This fibrosis, formed as previously described, ultimately contracts, and on the one hand causes atrophic changes in the liver cells, and on the other obstruction and obliteration of some of the interlobular and intralobular branches of the portal vein; this latter, though it contributes to, is not the sole cause of, the ascites—other important factors being the aforementioned new circulatory conditions, especially certain noteworthy changes in the hepatic arterial supply (that need not be further discussed here). Ultimately the potentiality for regeneration possessed by the liver cells and manifested to a remarkable degree, not only in the early but also in the late stages, gradually lessens and is finally lost, the general functional capacity of the liver cells being meanwhile compromised by the contracting connective tissue; the degenerative changes predominate over the regenerative, and the patient soon dies, if he has not succumbed earlier to an accidental infection to which his depressed vitality renders him especially susceptible.

The conspicuous change in the cirrhotic liver at necropsy, then, is the evidences of regeneration of the liver parenchyma; the evidences of degeneration, though sufficiently manifest in early cases, in advanced cases are commonly past and represented only by the newly formed and rearranged liver tissue and the fibrosis; and the liver as a whole may be said to represent its, for a time at least, partially successful efforts to compensate the consequences of the continuous or intermittent activity of the etiological factor—usually a poison, though in some cases possibly a substance causing thrombosis of the portal or hepatic artery radicles.

The idea of the primary change in cirrhosis being in the parenchymatous tissue is by no means new. It was entertained many years ago by Frerichs,[1] Ackermann,[2] Orth[3] and others, and, indeed, Laënnec,[4] who originated the term, was not altogether wrong when he looked upon the "granules" as new-growth, though they can scarcely be considered neoplasms, as he believed; the likelihood or possibility of the primary changes being in the parenchymatous tissue is conceded by Ziegler,[5] Rolleston[6] and others; its probability is suggested by the results of the work of the many observers who have studied the subject experimentally; it has recently been insisted upon by Kretz, Böstrom, and MacCallum, and it seems rather conclusively to have been proved recently by Pearce—who, experimenting with hæmagglutinative serums produced primary focal or widespread necrosis (depending upon the dose of the serum employed) with consecutive repair on the part of the liver cells and other changes that much resemble, though they are not identical with, cirrhosis as seen in man.

It behooves us, therefore, to discountenance, as far as possible, the use of the terms atrophic and hypertrophic, since a large liver may be atrophic to a noteworthy degree, and hypertrophy of the liver cells is a conspicuous feature of all small livers. Difficulties in the way of a satisfactory classification, however, are many, of which not the least important is the fact that different etiological factors may cause similar changes in the liver (so-called atrophic cirrhosis with and without antecedent alcoholism), that one factor may give rise to different forms, so-called, of cirrhosis (thus, so-called atrophic cirrhosis, fatty cirrhosis, and hypertrophic cirrhosis may be preceded by definite alcoholism), and that many factors may be operative in the one case. Probably heretofore we have been too much concerned with the size of the liver, which, nevertheless, is a conspicuous clinical feature; but progress is more likely to be achieved by search for the etiological factor than by too much attention to more or less disquieting clinical signs; and we have reason for believing that an organ like the liver which possesses really remarkable inherent capabilities for repair might, although considerably damaged, be able to establish functional sufficiency were the etiological factor, whatever it may be, corrected or removed early —rather earlier, however, than the disease is usually recognized at the present time.

[1] Klinik der Leberkrankheiten, 1861, Bd. ii. p. 19, and Atlas (also Translation by the New Sydenham Society).

[2] Ueber hypertrophische und atrophische Lebercirrhose, Virchow's Archiv, 1880, Bd; lxxx. p. 396; Die Histogenese und Histologie der Lebercirrhose, Virchow's Archiv, 1889, Bd. cxv. p. 216.

[3] Lehrbuch der spec. path. Anatomie, 1887, Bd. i. p. 939.

[4] Traité de l'auscultation médiate, 1819, tome i. p. 368.

[5] Lehrbuch der allg. Pathologie und path. Anatomie, 1898, 9te Aufl., Bd. ii. p. 591.

[6] Diseases of the Liver, Gall-bladder, and Bile-ducts, 1905, p. 196.

A CASE OF CONGENITAL HEPATOPTOSIS, SHOWING A MESOHEPAR.*

By Thomas Wood Clarke, M.D.,
RESIDENT PHYSICIAN, LAKESIDE HOSPITAL,
AND
David H. Dolley, M.D.,
LATE RESIDENT PATHOLOGIST, LAKESIDE HOSPITAL, CLEVELAND, OHIO.

The condition recognized as hepatoptosis is one of some rarity about which much has been written. It was first described in a postmortem examination by Heister[1] in 1754, but his article has been overlooked until recently, the credit generally being given to Cantani,[2] an Italian, who reported a case in 1866. Since his time the literature has been searched and collections of cases made by several authors, among whom may be mentioned Wickham Legg,[3] in 1878, with 20 cases; Faure,[4] in 1892, with 54 cases; Graham,[5] of Toronto, in 1895, with 68 cases, and, finally, Ssaweljew,[6] in 1903, who brings the subject practically up to date with 117 cases. Exhaustive discussions are numerous, the theses of Baget,[7] Duverney,[8] Haenselt,[9] and Pellet,[10] with the recent article of Teleky,[11] being the most complete.

By the term hepatoptosis, or floating liver, is meant a complete dislocation of the liver from its position under the diaphragm, and it does not include cases of floating lobe in which a portion of the organ remains in its normal position. The condition must be a primary affection of the liver, and not the result of intrathoracic or subphrenic abscess or tumor.

Taking this definition as our premise, we find 118 cases of complete hepatoptosis on record, 117 of which are tabulated by Ssaweljew, and 1 reported since. As to the pathogenesis of the condition, leaving out the theory of Heister,[1] promulgated in 1754, that it was due to the will of God to prove His omnipotent power, it narrows down to elongation of the ligaments, stretching of the vena cava, and congenital malformation. The condition is prone to occur in any state of laxity of the abdominal walls and decrease of the intra-abdominal tension. The direct causes given are: sex, repeated pregnancies, especially associated with a pendulous abdomen, removal of tumors, tapping of ascites, trauma, overstrain, and tight lacing. An analysis of Ssaweljew's table shows that of his 117 cases 13 occurred in men, 103 in women, and 1 in a child. Of the women 93 were married and 10 single.

* Read before the Clinical and Pathological Section of the Cleveland Academy of Medicine, March 8, 1905.

One point in the etiology of hepatoptosis which has given rise to acrimonious discussion is the occurrence of a mesohepar. Meissner,[13] in 1869, reasoning from an analogy to floating spleen and kidney, strongly advocated on purely theoretical grounds the apposition of the two peritoneal reflections from the liver to the diaphragm, together with their lengthening as the chief factor in the etiology. His cases did not come to autopsy. Leopold,[13] in 1874, and Sutuguin,[14] in 1875, accepted Meissner's theory, but advanced nothing to prove it. In 1885 Landau,[15] basing his statement on the negative results of a large number of postmortem examinations, particularly in infants, denied the occurrence of such a structure. Faure, in his classic monograph, published in 1892, dubs Meissner's theory a pure hypothesis, and insists that it be not considered. Later writers seem to have unanimously accepted Faure's ideas.

Malformations of the liver of any grade, excepting in monsters, are rare. Numerous cases are reported in which the anomalies consist in absence of one or more ligaments, multiple lobulation, hypertrophy, atrophy, or absence of various lobes, accessory lobes, or faulty position due to rotation about an axis. More marked defects are associated with umbilical or diaphragmatic hernia.

The case we report, Louisa L., a native-born American woman, aged thirty-four years, and unmarried, was admitted to Lakeside Hospital (medical number 3854) on November 4, 1903, on the service of Dr. Powell, to whom we wish to express our thanks for permission to report the case.

The patient was admitted for pain and swelling in the right knee and ankle. In the family history the mother died of "liver trouble," and one sister of dropsy, following rheumatism. The family history beyond this was unimportant. In childhood she had had measles, mumps, and chickenpox. There was no history of pulmonary, cardiac, or gastric trouble. The appetite was good. She had always been somewhat constipated. The menstruation began at thirteen years, and had always been regular, though scanty, until three months before admission, when it stopped. She had never been pregnant. She admitted leucorrhœa for the past three or four years, but indignantly denied the possibility of venereal infection. The condition for which the patient was admitted, a subacute rheumatism, has no bearing on the present report. She had never had a serious accident or fall, and said she did not use tight corsets. Nine years before admission she first noticed a tumor in the right side of her abdomen, about the size of her fist. This did not increase in size for two years and gave her no trouble. Since then she thinks it has increased slightly and caused some dragging pain. Three years before admission an exploratory laparotomy was made by a well-known Cleveland surgeon, who diagnosed "sarcoma of the liver (?)" and backed out. Since then the mass has given her no

FIG. 1

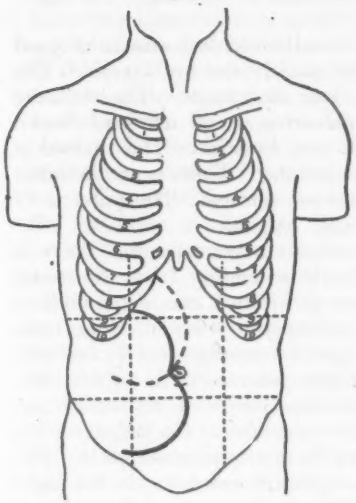


FIG. 1.—Palpation; patient on back. Black = position normally. Dotted = position with liver pushed up.

FIG. 2

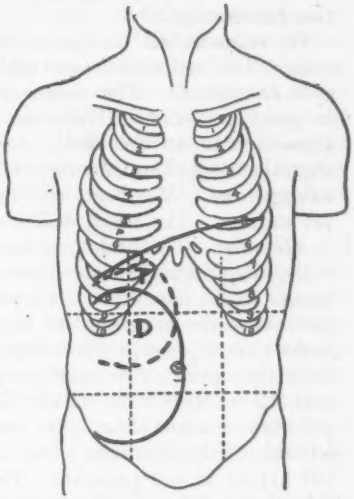


FIG. 2.—Percussion; patient on back. Black = natural position. Dotted = liver pushed up. P = pulmonary resonance. D = dulness. T = area of tympany between P and D.

FIG. 3

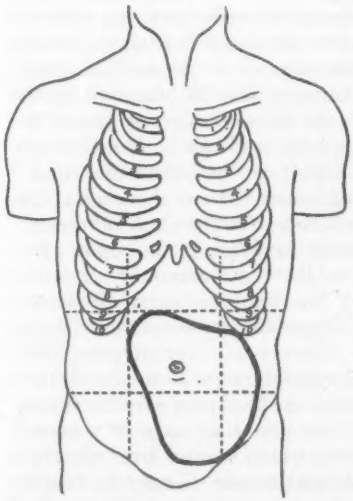


FIG. 3.—Palpation and percussion; patient on left side; position of liver.

FIG. 4

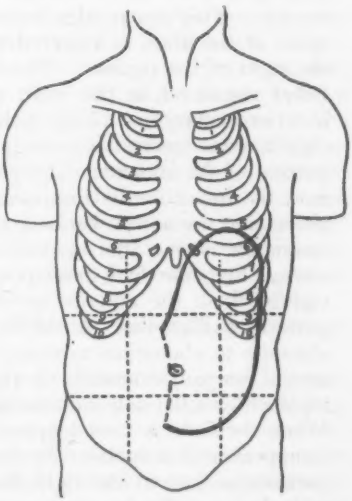


FIG. 4.—Gastric tympany; patient on back.

trouble, except for dragging pains at times on walking. The digestion has been good.

On examination the patient is a well-nourished woman of good color. The conjunctivæ are slightly muddy, but not icteroid. The eyes are normal. The tongue is clean and moist. The teeth are in good condition. There are numerous small areas of brown pigmentation on the cheek, neck, and forearm. The thyroid is slightly enlarged and the right lobe nodular. There is no glandular enlargement. The heart and lungs are normal. The pulse is 72 per minute. The vessel wall is easily palpable.

Abdomen. The abdomen is markedly asymmetrical. There is a definite bulging in the right flank, extending from the costal border to the iliac crest. It reaches to within 2 cm. of the midline just above the navel and to the midline just below it. The mass looks smooth, except for a slight groove running directly laterally from the navel. The most prominent point is 5 cm. to the right and 2.5 cm. below the navel. The mass moves on respiration; no pulsation is seen; there is no visible peristalsis. On palpation the left side of the abdomen is soft and there are no masses felt. The left kidney is just palpable. The spleen is not felt. In the right side of the abdomen (the patient lying on her back) is felt a large, smooth, elastic mass, extending from the midline to the extreme flank. This is easily movable and can be raised by pressure in the right flank. Along the midline of the abdomen it has a definite, sharp, overhanging edge, in which, just to the right of the navel, is a distinct notch. A similar edge can be felt along the lower border. This sharp edge runs from the right anterior superior spine of the ilium in a curved line to the costal border, 4.5 cm. to the right of the midline. The mass extends in the midline 7 cm. below the navel, in the right mammary line 16 cm., and in the anterior axillary line 12 cm. below the costal border, or just to the right anterior spine. It is easily movable and can be forced to any portion of the abdomen. By pressure it can be forced upward 5.5 cm., the upper border disappearing under the costal margin. On percussion the note is flat over the tumor. In the chest pulmonary resonance reaches the seventh costal cartilage in the right parasternal line, the sixth interspace in the right mammary line, the eighth rib in the anterior axillary line, and the ninth rib in the posterior axillary line. At this line the pulmonary resonance changes abruptly to abdominal tympany. There is no liver dulness. The area of tympany extends in the right mammary line 3 cm., and is then replaced by a flat note continuous with the dull area over the tumor. When the liver is forced upward this abnormal area of tympany disappears and is replaced by dulness, which reaches from the right parasternal line to the right flank and comes directly in contact with the area of pulmonary resonance.

By placing the patient on the left side the mass falls to the left

and leaves the right costal border. It then extends from the left Poupart's ligament to a point 2 cm. below the right costal border, a total distance of 24 cm., and has a width at the navel of 18 cm. In this position the left border can be easily felt in the left iliac fossa, and the sharp edge can be picked up between the thumb and finger. In this position the right border can be felt 9 cm. to the right of the navel, and is round, firm, and obtuse. From the upper right border of the mass there is felt a resistance running under the right costal border, resembling a ligament or pedicle, connecting the mass with the structures of the right hypochondrium.

On dilating the stomach by means of sodium bicarbonate and tartaric acid a prominence appears in the lower abdomen, most marked 4.5 cm. to the left and below the navel. The stomach tympany elicited by percussion and auscultatory percussion begins at the fifth interspace in the left parasternal line and extends throughout the left abdomen to a point 8 cm. below the navel in the midline, and to within 4 cm. of the left anterior superior spine of the ilium. To the right of the midline the area of tympany is encroached upon by the flatness of the tumor mass. The right kidney is indefinitely palpable in its normal position.

Vaginal examination shows a small retroflexed uterus, and no connection between the pelvic organs and the tumor mass.

There is marked swelling and tenderness of the right knee and ankle. The right heel is prominent, hard, and sensitive. The shins are clear; there is no œdema. The knee-jerks are normal.

Examination of the blood and urine shows nothing abnormal.

The patient received treatment for her joint trouble from November 4, 1903, to January 23, 1904, with marked improvement. Nothing was done for the liver condition, as it was giving her no trouble, until January 18th, when, on the possibility of the tumor being a gumma, potassium iodide was started in increasing doses. The temperature, pulse, and respiration all remained normal until January 24th, when, with a complaint of pain over the tumor, the temperature rose to 101° and the pulse to 100. The pain increased markedly during the next four days; the temperature rose to 104°; the pulse to 124, and the respirations to 130. An exploratory operation was performed by Dr. Dudley P. Allen on January 29th, and an acute appendicitis found.

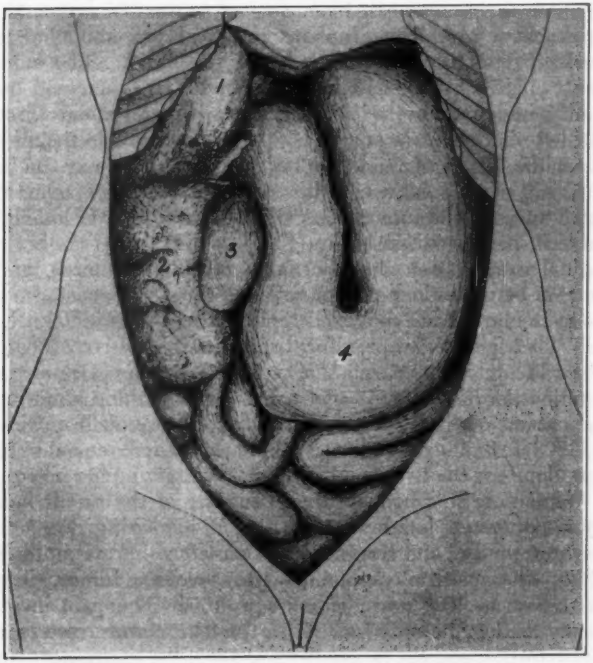
The patient died February 4, 1904. An autopsy was performed the same day.

The point of special interest in the clinical history of this case is the total absence of the accepted etiological factors in floating liver. The patient had never been pregnant, had had no accident, and had not been a heavy worker. Her abdominal walls were not especially lax. The etiological factor could not be determined during life, and the autopsy findings were required to demonstrate it as a case of congenital hepatoptosis.

Pathological Report. The following extracts are made from the autopsy protocol. The autopsy was performed two hours after death.) The body is that of an emaciated white female, 158 cm. long, with beginning rigor mortis.

The liver is displaced, lying entirely on the right side. It has two lobes—an upper, corresponding to the left, and a lower, corresponding to the right. Each lobe has a flattened and blunt, ovoid shape, the lower being nearly double the size of the upper. It

FIG. 5

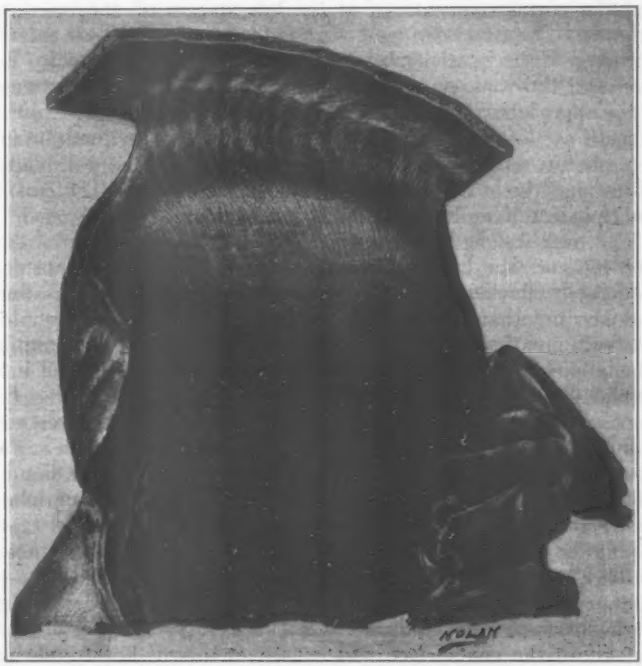


Abdomen at autopsy: 1, upper (left) lobe of liver; 2, lower (right) lobe of liver; 3, gall-bladder; 4, stomach.

extends 9.5 cm. below the xiphoid cartilage, 8 cm. below the costal margin in the mammary line, and 5.5 cm. in the anterior axillary line. The two lobes are united by an isthmus of dense fibrous tissue, which varies in width from 1.5 cm. on the right side to 3 cm. on the left, and averages 5 mm. in thickness. Scattered throughout this isthmus are isolated liver lobules, some of which are fatty. The lower lobe possesses no ligamentous attachment. The right lateral and coronary ligaments are entirely lacking. Limited to

the upper margin of the upper lobe there is a double reflection of peritoneum to the diaphragm. The liver itself does not touch the diaphragm, and the mesohepar thus formed is 13 mm. in length. The two peritoneal reflections are united only at their free edges, enclosing a space 1 cm. in width at the surface of the liver and a few millimetres at the diaphragm, which is filled with lax fibrous tissue. From the upper half of the right margin of the upper lobe, along the natural line of reflection of the left lateral ligament, there extend

FIG. 6



Upper lobe, showing attachment to diaphragm by mesohepar.

lax and easily torn fibres to the diaphragm. These are regarded as adhesions. The suspensory ligament, instead of being attached along the longitudinal fissure, touches the interlobar isthmus only at its left margin, but it is also attached along the left border of the upper lobe. The round ligament also joins the interlobar isthmus at its left margin. A thick zone of fibrous and fatty tissue, with isolated nodes of liver parenchyma, lies posterior to the junction of the suspensory ligament with the upper lobe. The hepatorenal fold of peritoneum joins the liver at the interlobar isthmus.

The fissure of the gall-bladder appears as an ovoid depression, 4 cm. long, in its normal position with reference to the lower lobe, but its long axis coincides with the long axis of the lobe. The transverse fissure is represented by a deep notch in the upper posterior margin of the lower lobe, from which two fissures branch at an acute angle. The left branch, which is 4 cm. long, is parallel to the gall-bladder fissure and 1.5 cm. from it. The right branch, which is longer, is poorly defined at its origin, but deep at its extremiyt. The subdivisions of the right branch of the portal enter these fissures. The hepatic ducts leave the liver and the hepatic artery and the portal vein enter it at the left margin of the interlobar isthmus. The artery divides 4 cm. and the vein 5 cm. before entering the liver. The relative position of these vessels is normal. The fissure of the vena cava crosses the left posterior upper extremity of the upper lobe. The umbilical fissure and the fissure of the ductus venosus are lost in the separation of the lobes. The quadrate lobe is probably represented by the portion between the gall-bladder fissure and the left branch of the transverse fissure. The caudate and Spigelian lobes have necessarily no analogues.

The liver weighs 1385 grams. The upper lobe measures 13.8x 10.8 x 6 cm., the lower 17.5 x 11.5 x 8 cm. The liver capsule is moderately thickened. The surface of the lower lobe is finely nodular, but that of the upper is more smooth. The lower lobe cuts with greatly increased resistance, and its cut surface is granular. The lobules vary much in size. There is a distinct increase of interlobular fibrous tissue. The liver tissue is of a dull brownish-yellow color. Over the surface and throughout the organ are scattered minute bright-yellow areas. The upper lobe has a smooth surface on section, its resistance is but slightly increased, and the tissue is flabby in consistence. Occupying the centre of the upper lobe is an irregular mass of mixed pearly and translucent fibrous tissue, having the shape of a three-pointed star. One point extends nearly to the left margin, while the other two extend only half-way to the right. Throughout the mass are scattered irregular nodules, varying in size from a few millimetres to 1 cm. in diameter. These project above the cut surface and consist of a firm but friable and structureless tissue of a homogeneous yellow color.

The gall-bladder, which is much enlarged, is U-shaped, and lies between the stomach and the lower lobe of the liver. The distal arm, which is more distended, lies anteriorly. It is 9 cm. long and 5 cm. in diameter. The proximal arm is the same length, but gradually narrows to the orifice of the cystic duct. The organ is not adherent.

The stomach also has a U-shape and is enormously dilated. It extends 11 cm. below the xiphoid cartilage. The cardiac arm of the U measures 22.5 cm. in length and the pyloric arm 16.5 cm. The diameter at the cardiac end is 19 cm., at the middle 9.5 cm., from which the size diminishes gradually to the pylorus. The pylorus is in its normal position.

The appendix is absent and closure of the wound of operation is not perfect, intestinal contents exuding from a minute hole. In the right ileocæcal region the intestinal surfaces are united by fibrinous exudate and have a dark necrotic appearance. Similar exudate is found in moderate amount over the liver and the spleen. There is a scanty amount of brownish, turbid fluid free in the peritoneal cavity. The transverse colon is prolapsed and collapsed, and lies behind both liver and stomach.

The mucosa of an area, with a diameter of 4 to 6 cm. about the orifice of the appendix, is ulcerated. The ulcers have an irregular shape, with a sloping edge and a necrotic floor. The intervening tissue is intensely congested. The mucosa of the rest of the cæcum and colon is smooth, but indurated and mottled with dark-brown pigmentation. The remaining viscera are normal in their positions.

Microscopic. Sections from the new-formed tissue in the upper lobe of the liver show typical gummata. The periportal tissue is especially increased in the lower lobe, with atrophy and necrosis of the liver cells. Periarteritis and endarteritis are well marked.

There are extensive areas of coagulation necrosis and purulent infiltration in the mucosa and submucosa of the cæcum. Some ulcers extend to the submucosa. The acute process is so well marked as to obscure any old lesions, but in the submucosa of the colon are areas of vascular and well-organized granulation tissue, with extensive proliferation of the adventitia of the small arterioles. Some larger arterioles are occluded by a recent endarteritis. An enormous amount of a coarse brownish pigment is deposited in the mucosa of the large intestine, both in cells and free. It does not give an iron reaction.

Pathological Diagnosis. Congenital malformation and displacement of the liver; multiple gummata of the liver, with syphilitic cirrhosis; chronic passive congestion of the portal system; operative removal of the appendix; acute general peritonitis; dilatation of the stomach with atrophic gastritis; acute ulcerative typhlitis; chronic enterocolitis; syphilitic endarteritis and periarteritis of the large intestine; hypertrophy of the thyroid; tuberculosis of the tracheal glands.

We are indebted to Dr. W. T. Howard, Jr., for the use of material and for his supervision of the work.

Conclusions. 1. The abnormal position of the liver, with its limited mobility, its atypical shape, the absence of the coronary and right lateral ligaments, the abnormal origin of the left lateral ligament, which assumes the function of the coronary ligament, and of the suspensory and round ligaments, the shifting of the fissure of the vena cava from one lobe to the other, though the course of the vessel is normal, together with other variations, leave no doubt as to the embryonic origin of the condition. Syphilis was merely a coincidence.

2. As the review of the literature, particularly of the references given in the *Anatomischer Anzeiger* for the past fifteen years, and of the collections of Jacquemot[16] and Faure,[4] shows no identical case, and but one slightly resembling the present one, it must be considered as unique.

3. The case, though it does not prove that a mesohepar is the cause of hepatoptosis, does prove Meissner's hypothesis that such a condition may exist.

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CHRONIC PARENCHYMATOUS NEPHRITIS; ACUTE GENERAL INFECTION; INFARCTION OF THE LUNG; DOUBLE PHLEBITIS; NEPHROLITHIASIS; PARTIAL RECOVERY.

BY CARY B. GAMBLE, JR., A.M., M.D.,

ASSOCIATE PROFESSOR OF CLINICAL MEDICINE, COLLEGE OF PHYSICIANS AND SURGEONS, BALTIMORE, MD.

GEORGE H., aged thirty-nine years; white; married; consulted me on April 20, 1904, on account of albuminuria. His family history was negative. He had had no sickness of any sort since childhood, except that six weeks previously he had suffered from a pharyngitis, which lasted for a week, and which possibly was of importance, as he had been in contact with a scarlet-fever patient. His throat, however, healed promptly and he felt very well afterward. His habits had always been good; he had never been an alcoholic, although for several years had been accustomed to drink two bottles of domestic beer at night; he had used tobacco in moderation. He lived in Baltimore, but his place of business was in Washington, so that it was necessary for him to get up at 6 o'clock in the morning in order to take the 7 o'clock train for that city, returning in the evening. This mode of life had been followed for eight years,

and he was always in a hurry going in the morning and coming back in the evening. He was in the habit of sitting up late at night, and frequently did not get enough sleep. Shortly before he consulted me he noticed that he became fatigued after slight exertion and that he had shortness of breath. An examination of his urine at that time showed a large amount of albumin; the specific gravity was 1012. The amount passed in the twenty-four hours seemed to be normal, but no accurate record on this last point had been kept. On microscopic examination granular, epithelial, and hyaline casts were found, but not in great numbers.

Physical Examination. Medium-sized, well-nourished man; pallor marked; no œdema of the face or extremities; chest broad, expansion good and equal; lungs clear. *Heart:* Apex in normal position, sounds soft, distant; no accentuation; the bloodvessels are somewhat thickened, but are easily compressed; tension normal. The patient has a remarkable degree of self-control; he is not nervous, and informs me that, except for his weakness and shortness of breath, he never felt better than he does now. Blood count: 3,500,000 reds; leukocytes, 10,000; blood pressure, 140; temperature normal. He was put to bed, but, as the amount of albumin increased and he developed œdema of the legs, he was taken to the Union Protestant Infirmary.

May 2d. The patient complains of a violent pain in the left side of the chest under the eighth rib behind. Over this area there is heard a localized pleural rub, with slight increased conduction of the voice and breath sounds.

4th. The pain has disappeared; the color has improved; 800 c.c. of urine were voided in the last twenty-four hours; specific gravity, 1022; white blood count, 5000; blood negative for malaria; hæmoglobin 90 per cent.

6th. Has had a restless night and feels much worse; his pulse is rapid, and his urine shows more albumin than for several days. Numerous rales are heard throughout the lungs and the aortic second sound is accentuated; the heart's action is rapid and weak. The swelling about the ankles is diminishing.

9th. The patient has complained of a pain in his right side behind. A friction rub, with increased conduction of voice and breath sounds, is present over an area beginning at an imaginary line two inches to the left of the spine and extending from the eighth to the tenth ribs. A few crackling rales are heard at each base.

10th. During the night the left thigh suddenly became swollen and the patient complained of a good deal of pain in the groin. The veins of the left leg are distended and a mass can be felt just below Poupart's ligament; for the last few days the patient has had a slightly elevated temperature.

12th. The whole left leg is much swollen; there is no œdema of the right leg; the veins of the left leg are palpable at the saphenous

opening and the toes are blue; there is swelling of the scrotum and penis; the friction rub noted on the ninth has disappeared. By night the swelling in the leg had increased and muscular contractions in the calf muscles had appeared. The patient looked like a very ill man; his face was pinched; he was much depressed and very weak.

13th. His condition has steadily grown worse; muscular contractions are frequent; in the last twenty-four hours he has passed only 520 c.c. of urine; the penis and scrotum are enormously swollen; the pulse is rapid and of poor volume. The blood count shows 13,800 leukocytes; the blood pressure is 130. Considering his extremely grave condition, Dr. Finney and I decided it would be well to try decapsulation of the kidneys. This was done at 3 P.M. The patient was put to sleep and a strip taken from the capsule of each kidney. The left kidney was slightly larger than normal; the right kidney much larger. Chloroform was employed for anæsthesia. The patient regained consciousness quickly and by midnight is feeling comfortable. There is no pain in the leg; some few rales are heard over the chest; the pulse is full, strong, and regular; the muscular contractions have disappeared, and apparently there has been a slight increase in the amount of urine passed; the general condition seems better.

14th. The patient slept well last night; the pulse is somewhat improved, but the patient is exhausted; he does not complain of pain in the regions of the incision; the left leg is swollen, but does not inconvenience him. The leukocytes have increased to 16,800. During the next few days his general condition improved, but there was no diminution in the œdema, the amount of albumin passed or the number of casts seen on microscopic examination. The wounds in the back healed promptly.

From May 27th the œdema rapidly increased, so that on June 1st the scrotum was tapped in five or six places, with the loss of a large amount of fluid. During this month his condition remained practically about the same, except that his strength improved, and toward the last of the month he was kept out-of-doors.

From July 1st there was a gradual increase in the general œdema, so that by the 16th he was practically waterlogged. On that date his legs were scarified in three places each, with the loss of a great deal of fluid. An attempt was made to tap the abdomen, but without success, as there was no free fluid in the cavity. The draining was very effectual and the legs, scrotum, and penis slowly came back to normal size.

During August his condition was about the same. After the openings in the legs closed the swelling came back, so that by the 16th it was necessary to scarify the legs and scrotum, which again relieved him.

August 27th. The patient began to suffer from an attack of pain and swelling in the right leg, similar to that which he had had in the

left. The veins became prominent and he suffered a great deal for two days.

31*st*. The condition has improved. Liver dulness begins at the lower border of the sixth rib, and the edge is palpable two fingers' breadth below the costal margin; his right leg is swollen, the veins are prominent, and he complains of considerable discomfort.

September 7th. Patient left the hospital to-day; his legs have not been draining for the past three days; there is no œdema about the body and he feels better; the scrotum has diminished in size; the patient eats and sleeps well. Toward the end of the month it was again necessary to scarify the legs, and again the procedure proved beneficial; the œdema went down and the wounds healed, so that by November 4th there was no discharge. Again the œdema increased, and he was tapped on November 10th, with slight improvement. He was at a standstill until November 20th, when he was taken with colicky pains in the region of the right kidney. With the attack there was an increase in the amount of urine, the daily average for the first week being 1400 c.c. The kidney pain was as severe, but paroxysmal. At the end of a week he commenced to pass small calculi, phosphatic in nature, and the pain stopped. On the next the left kidney was attacked and the amount of urine dropped steadily. On the fourth day the pain disappeared and only 30 c.c. of urine were passed. The next day the patient was somnolent, he had no pain, his pulse was rapid, of fairly good volume, and the œdema was increasing. He was bled, eighteen ounces being removed, and in the next twenty-four hours he passed a large amount of urine, with a specific gravity of 1008 and an abundance of albumin. The amount of urine gradually decreased, but the œdema disappeared. In two weeks' time the swelling commenced again and extended up from his feet, involving his whole body and face. The legs were again tapped, with but little effect.

December 14th. General condition not good; swelling of the face and body marked.

15*th*. He was placed on a salt-free diet, and in the next few days there was a remarkable change for the better. The œdema rapidly decreased; the thirst, which before had been intense, left him entirely; the mouth became moist and the general condition improved greatly. After the first week the amount of urine passed fell, but in proportion to the fluid taken was greater than it had ever been, and from that time on the patient made a steady improvement, so far as subjective symptoms were concerned, although the amount of albumin in his urine remained high.

He is now, November 1, 1905, passing a normal amount of urine, with a specific gravity around 1030; 0.3 per cent. albumin; he is actively engaged in business and feels strong and well. Toward evening he has a slight amount of swelling about his ankles, especially in his left leg, which is possibly due to his old phlebitis. He has prac-

tically become a vegetarian, as the taste of meat without salt is most distasteful to him. On two or three occasions he has used salt in his food, and, feeling badly afterward, has determined never to take any more unless the craving for it is irresistible.

During the five months that this man was in the hospital a daily record was kept in which were specified the fluid intake, the amount of urine passed, the amount of nitrogen output, and the percentage of albumin. Since leaving the hospital the total amount of fluid taken and the amount of urine passed have been recorded.

As to the total amount of nitrogen: This varied somewhat, but on the whole did not teach us much. After the Edebohls operation on May 13, 1904, coincident with the rise in the amount of urine, there was a very decided rise in the output of nitrogen, the amount being about double for the first four days that excreted before the operation. At the same time there was a fall in the percentage of albumin, although the total amount of albumin excreted remained the same. All through his attack, however, there was at no time any fall in the amount of nitrogen excreted, except in proportion to the amount taken in, and it is interesting to note that only once was there a threatening of uræmia, namely, after the suppression of urine that came with the attack of kidney stone.

The *albumin* was and has remained persistently high and has been excreted in about the same amount.

Casts were never numerous, but always to be found.

The amount of urine passed in comparison with the amount of fluid taken showed one particularly interesting point. Before the salt-free diet was instituted the amount of fluid taken was on a par with or somewhat in excess of the amount of the urine output; but afterward the intake was only one-half of the output.

The *blood pressure* was never higher than 160, and usually remained around 130 mm.

No accentuation of the aortic second sound has ever been noted.

Treatment. For the first five weeks von Noorden's idea as to diet was followed. The milk was modified to contain a low percentage of proteid, and calcium carbonate was given with each portion. From this procedure no apparent result was obtained, the amount of albumin passed in the twenty-four hours remaining constant. As was to be expected, the total amount of nitrogen fell, but only in proportion to the amount of the nitrogen intake. Although there was no betterment in the condition of the kidneys as the result of this diet, it should be remembered that we had, in addition to the chronic condition, an acute infection. After the first five weeks the patient was given broths without meat, a small amount of starchy food, and unmodified milk.

Water. During the first part of the treatment lithia water and distilled water were used in large quantities, but it soon became apparent that the kidneys could not bear over a certain amount

and a restriction was placed upon the fluid intake. It was noted several times that when over a certain amount of water was given the œdema increased and the amount of urine was diminished; whereas after the amount of water was cut down the œdema diminished and the amount of urine output increased.

Drugs. Of the diuretics he was given infusion of digitalis, potassium citrate, tincture of iron, buchu, diuretin, with alkalies and squills. Of these, syrup of squills seemed to have some but only a temporary effect. Half a teaspoonful was given four times a day, and a study of the urine in Table I. before and after its administration shows that there was apparently a decided increase in the amount of urine passed; certainly the œdema was diminished. This drug was used over a period of two weeks, and when it began to lose its effect it was stopped. It caused no nausea and no depression. No results could be directly ascribed to the action of the other drugs; in fact, they seemed to do harm, especially digitalis. Magnesium sulphate was given frequently, and, by acting on the intestine, drained off a certain amount of fluid, but it did not increase the amount of urine passed. Elaterium was used twice, with no good effect, and it caused a good deal of pain. A pill composed of calomel, digitalis, and squills acted badly, the calomel causing an increase in the amount of albumin and a fall in the amount of urine.

The only two drugs that seemed to benefit him at all, then, were squills and the aperients, and it is to be remembered that the squills was used at the same time that the scrotum was tapped. This drug was tried again and had no effect in increasing the amount of urine passed.

In contrast with the effects of the drugs those resulting from what may be called *mechanical agents* were most striking. *Tapping the scrotum* not only relieved the œdema considerably, but a study of the table will show a direct increase in the amount of urine secreted. The same result followed tapping the legs, the resulting drainage being most profuse, except on the last occasion. Scarification of the scrotum was practised twice, the first time being followed by most noteworthy results.

THE EDEBOHLS OPERATION. The result was disappointing in some respects. The amount of urine increased considerably for a few days, but the œdema did not diminish, and during that period the patient was getting a larger amount of fluid than usual. On the day of operation and the one following the patient was given subcutaneous injections of salt solution. It was noticed when these were given that they were absorbed slowly. This fact is easily understood, and the employment of this procedure was certainly a therapeutic error; there was an increase in the amount of urine passed, but the intake of fluids was out of proportion to that amount.

The patient's general condition improved very much after the operation. He lost what he had had before in a marked degree—a

septic look—and his leukocyte count increased considerably. When the capsule of his kidneys was detached there was more pressure than usual. The kidneys welled up out of the wounds as if pressure had been removed.

The patient relapsed into his former state, so far as the condition of the kidneys went, in a very few days, and no sign of kidney betterment could be noted, the amount of albumin being increased. For the first four days after the operation the nitrogen output was doubled, but it is more than probable that this change would have taken place in a normal individual after an operation. The following table shows the amount of urine passed and the amount of fluid taken before decapsulation of the kidneys, while he was taking the squills and after the scrotum was tapped for the first time:

TABLE I.

	Amount of urine passed.	Amount of fluid taken.		Amount of urine passed.	Amount of fluid taken.
May 10	1368 c.c.	3250 c.c.	May 28	760 c.c.	1400 c.c.
" 11	1000 "	1875 "	" 29	1000 "	1800 " [2]
" 12	840 "	2000 "	" 30	1000 "	1800 "
" 13	520 "	2300 " [1]	" 31	1700 "	2000 " [3]
" 14	1510 "	1800 "	June 1	1400 "	1560 "
" 15	1240 "	1500 "	" 2	3130 "	1500 "
" 16	1300 "	1700 "	" 3	1650 "	1510 "
" 17	1300 "	1600 "	" 4	2200 "	1020 "
" 18	1780 "	2000 "	" 5	1570 "	1000 "
" 19	1740 "	1500 "	" 6	1300 "	1250 "
" 20	1030 "	1800 "	" 7	1190 "	750 "
" 21	1290 "	1800 "	" 8	2440 "	800 "
" 22	1410 "	1600 "	" 9	1430 "	490 "
" 23	1450 "	1600 "	" 10	1580 "	1020 "
" 24	1430 "	1600 "	" 11	1560 "	1000 "
" 25	1450 "	1430 "	" 12	1360 "	1000 "
" 26	1020 "	1440 "	" 13	870 "	750 " [4]
" 27	1180 "	1440 "	" 14	800 "	490 "

[1] Operation, decapsulation both kidneys.
[2] Squills.
[3] Scrotum tapped.
[4] Squills stopped.

For increasing diuresis venesection showed the most remarkable results. For the first time in the course of the illness the amount of urine passed was sufficient to drain away all the œdema. In this connection it would seem almost justifiable to think that there might have been the same increase after decapsulation had salt solution not been used; for, after all, venesection acts on an engorged kidney by relieving tension. The effect of venesection was not prolonged, but while it lasted it was certainly very remarkable. As was mentioned above, the procedure was resorted to for almost complete suppression of the urine following an attack of nephrolithiasis, and a study of this chart shows that the mechanical irritation exerted by the stones as long as only one kidney was involved produced a diuresis of considerable amount; but that when the second kidney became affected there was almost complete suppression of the urine, followed by the polyuria after the bloodletting.

TABLE II.

	Amount of urine passed.	Amount of fluid taken.		Amount of urine passed.	Amount of fluid taken.
Oct. 29	570 c.c.	550 c.c.[1]	Nov. 11	330 c.c.	200 c.c.[4]
" 30	570 "	510 "	" 12	180 "	720 "
" 31	730 "	660 "	" 13	30 "	390 "[5]
Nov. 1	1270 "	850 "	" 14	4590 "	1580 "
" 2	1110 "	900 "[2]	" 15	6720 "	2550 "
" 3	1120 "	830 "[3]	" 16	2880 "	1050 "
" 4	1020 "	630 "	" 17	1940 "	1720 "
" 5	2160 "	960 "	" 18	1720 "	580 "
" 6	2370 "	1240 "	" 19	1825 "	820 "
" 7	970 "	670 "	" 20	1540 "	760 "
" 8	1200 "	860 "	" 21	1040 "	700 "
" 9	850 "	805 "	" 22	1230 "	900 "
" 10	460 "	640 "	" 23	1040 "	820 "

[1] Kidney colic, right kidney. [2] Kidney colic. [3] Kidney colic.
[4] Kidney colic, left kidney. [5] Venesection, 18 ounces.

The effect of the *salt-free diet* was interesting for several reasons. The results were more permanent than any obtained before. In the first place, it brought about from its use a reversal of the relation between the amount of fluid intake and the amount of urine excreted; but besides this there were several points that are well worth considering. Before taking this diet the patient had complained continuously of intense thirst, and to allay it was sipping water constantly. After salt was omitted from the food, and this was done absolutely as far as could be, the thirst disappeared, and the tongue and mucous membranes, instead of being dry, as they formerly were, became soft, and there was so marked an absence of thirst that the patient had to be directed to take a certain amount of fluid in order to prevent too heavy a burden upon the crippled kidneys. Moreover, he felt better soon after starting it than at any previous time during his illness, and his betterment has continued. He has found out himself that he is decidedly worse and that the œdema increases as soon as he goes back to salt in his food. As a result he has practically become almost a vegetarian, as he finds meat is very unpalatable without salt.

TABLE III.

	Amount of urine passed.	Amount of fluid taken.		Amount of urine passed.	Amount of fluid taken.
Dec. 10	1250 c.c.	1970 c.c.	Dec. 20	1010 c.c.	300 "
" 11	1190 "	1840 "	" 21	730 "	180 "
" 12	1120 "	1450 "	" 22	850 "	360 "
" 13	1230 "	1610 "	" 23	610 "	320 "
" 14	1170 "	1100 "[1]	" 24	771 "	420 "
" 15	2050 "	160 "	" 25	980 "	570 "
" 16	2190 "	160 "	" 26	960 "	410 "
" 17	2440 "	160 "	" 27	950 "	430 "
" 18	1650 "	240 "	" 28	610 "	320 "
" 19	1180 "	150 "	" 29	850 "	610 "

[1] Patient put on salt-free diet.

SUMMARY. *Diagnosis.* Chronic and parenchymatous nephritis; acute general infection resulting in infarction of the lungs; double phlebitis; nephrolithiasis of both kidneys.

Prognosis. On two occasions during the course of the year the patient was manifestly close to death: the first time just before the operation for decapsulation of the kidneys, and the second time after the attack of kidney colic, when there was almost complete suppression of the urine.

It is manifestly impossible to be at all sure about the outcome in this case, but the whole course of the disease shows that there must have been, and must be still, a certain amount of healthy kidney tissue left. Therefore, despite the desperate illness through which the man has passed, and despite the fact that the excretion of albumin and casts has not changed, one may venture to hope that there are an indefinite number of years before this man, during which he may live and possibly still do good work. My experience, especially of late years, has taught me the great uncertainty and wide variations in the course of kidney cases. No general rule can be laid down, but a complete study of the individual equation will sometimes help us in establishing a prognosis that will prove approximately correct.

So far as the treatment in this case is concerned, drugs exerted practically no effect, and the same may be said as regards diet, with the exception that exclusion of salt from all articles of food unquestionably had a great influence upon the œdema.

The Edebohls operation in this case was of doubtful utility. My impression is that it did no good beyond relieving tension at the time.

Venesection acted wonderfully as a diuretic, but produced no permanent result.

A last point, and one which is too often forgotten, is that patients suffering from parenchymatous nephritis are embarrassed rather than benefited by subcutaneous injections of salt solution. In fact, we are to be on our guard about using this procedure, because at times it may prove exceedingly dangerous.

FATAL OBLITERATING ENDOPHLEBITIS OF THE HEPATIC VEINS.

BY ALFRED F. HESS, M.D.,
OF NEW YORK.

(From Prof. Chiari's Pathologico-anatomical Institute, Prague.)

A DISEASE characterized by a gradual proliferation of the lining wall of the hepatic veins and resulting obstruction, with all its disastrous consequences to the liver and portal system, was men-

tioned for the first time by Budd in 1846 in his treatise on the liver. Since that time numerous similar cases have appeared in the literature, some 23 in all, the majority of which have been published in the last ten years. The German, French, Swiss, Italian, and English literature contains examples of this obliterating endophlebitis of the hepatic veins, but as yet no case has appeared in American scientific or clinical publications. We can hardly believe that cases of this nature have not at some time presented themselves in the clinics of our country. Moreover, when we consider that the outcome of the disease is invariably fatal, the conviction is strengthened that postmortem examinations upon such cases have also been made without the true cause of the pathological lesions and of death being disclosed. This is very easily explained and understood when we realize that, clinically, the cases mask themselves under the every-day garb of a Laennec cirrhosis, and, therefore, are not apt to attract particular consideration; and that at the autopsy, unless the hepatic portion of the inferior vena cava is opened, and the ostia of the hepatic veins there examined, the clinical diagnosis of cirrhosis of the liver may readily be declared to have been correct. To bring out more forcibly the point that this condition is overlooked, not only in the United States but elsewhere, and is by no means as rare as the paucity of reported cases would lead one to believe, let me call attention to the fact that five of the 23 cases below mentioned are reported from one pathological institute, that of Chiari, of Prague, and that since his thorough exposition of the subject, in 1899, two further cases have been found by him at autopsy. It is therefore to bring this condition to the notice of the clinician and pathologist that I publish a full report of a case of this disease. For I feel convinced that we cannot hope to obtain a clearer insight into its cause, or a recognition of its clinical aspects, except by a consideration of many more cases than have been studied and collated up to the present time. In order to give the reader a comprehensive idea of the symptomatology and pathology of a disease which is as yet so little known, I have prepared a tabular synopsis of all the cases which I have been able to find, and shall precede the report of the case which suggested the article, by a general survey of all the data at hand. The facts are in each case taken directly from the original reports, the evident omission of important data being due to lack of information furnished by the author.

Case.	Age and sex.	Clinical data.	Autopsy.	Microscopic data.	Conclusions of the author.
Budd, 1846	52 years ♂	.....	Hepatic veins thickened and containing a "pseudomembrane;" thrombosis of portal veins; adhesive perihepatitis, pericarditis, and pleuritis.	.....	No cause assigned for thickening of veins; the adhesive serositis attributed to irregular mode of life, probably alcoholism being meant.
Cohn, 1860	.....	.....	Widespread phlebitis of hepatic veins; thrombosis of portal veins; ascites; enlarged spleen.		
Frerichs (1), 1861	38 years ♀	Abdominal pain, sacculated peritoneal exudate, slight icterus, œdema of lower half of body.	Ostia of hepatic veins closed by complete or partly fenestrated septa and surrounded by thick connective-tissue sheath; liver smaller by a third, firmly bound down, the capsule thickened, sending firm bands into liver tissue.	....	The valve-like closure of hepatic veins due to a primary peritonitis causing a secondary perihepatitis with connective-tissue bands entering the liver tissue and pressing on the venous walls.
Frerichs (2)	45 years ♀	Ascites, diarrhœa, icterus, enlarged spleen.	One hepatic vein completely closed by a light red mass, the size of a cherry; one ending blind, with wall greatly thickened; a third containing adherent thrombi; the vena cava containing round plaques, its walls flattened together by connective-tissue bands; loosely attached thrombi in portal vein; liver somewhat small, connective-tissue masses on under surface, extending into parenchyma.	....	Adhesive phlebitis of hepatic veins due to chronic peritonitis.
Rosenblatt, 1867	27 years ♀	Sticking abdominal pain, ascites, distention of abdominal veins.	Ostia of hepatic veins entirely absent but represented by slight elevations and depressions of wall of vena cava; left lobe of liver tightly bound down, bands extending from capsule into parenchyma; primary carcinoma of liver with carcinomatous peritonitis.	.....	Hepatic veins obstructed as result of fetal hepatitis.
Gee, 1871	17 mos. ♀	Appeared to have abdominal pain; ascites.	Hepatic veins closed off from vena cava by thin membrane, showing merely shallow dimples at these sites, many filled with tough thrombi; liver somewhat small, tough, with perihepatitis; signs of compensatory circulation.	.....	Primary cirrhosis of liver, extending to capsule, especially about hepatic veins.
Schüppel, 1880	16 years ♀	Serofibrinous pleurisy, involving the right pleura (the only symptom mentioned).	Several hepatic veins of right lobe completely closed by organized thrombi; liver rather large; no perihepatitis: spleen very large; no ascites; organized thrombi in longitudinal sinus and both transverse sinuses of dura mater.	....	Possibly alteration of coagulability of blood, causing tendency to thrombosis.

Hainski, 1884	22 years ♂	Ill for one year. Diagnosis of chronic peritonitis with pressure on vena cava and bile-ducts by new growth of fibrous tissue.	Organized thrombi in hepatic veins, no large vein emptying into vena cava; the walls of hepatic veins and vena cava thickened and surrounded by connective tissue which extended into liver; liver somewhat small, especially the right lobe; tough, congested, granular, and containing grayish-brown nodules; moderate perihepatitis; ascites, chronic enlargement of spleen, purulent peritonitis.	The nodules were found to be due to circumscribed hyperplasias, in the nature of regenerative growth of parenchyma.	Obliteration of the hepatic veins following thrombosis; the primary lesion was a chronic peritonitis which caused cirrhosis.
Lange, 1886	39 years ♂	Gradual illness nine mos. after pregnancy, ascites, abdominal discomfort, anasarca, large liver; ill five and a half months in all.	Hepatic veins in liver appearing as connective-tissue bands, many absolutely obliterated, some containing thrombi; one at a point of juncture of two veins held a calcareous nodule the size of a cherry; the inferior vena cava showing longitudinal thickening and numerous ostia of hepatic veins blocked; some branches of portal vein outside of liver thickened; liver normal size, congested, showed dark red and circumscribed yellowish areas; localized peribepatitis on upper surface posteriorly; ascites.	Hepatic veins showed thickening of intima, and in places also of adventitia, concentric in arrangement; somewhere stenosed, many obliterated; liver was congested, showing some increase of connective tissue in yellowish areas.	Primary chronic endophlebitis of hepatic veins, possibly syphilitic, although nothing in the history or physical data suggesting syphilis.
Kelynack, 1897	32 years ♂	For two years abdominal pain, later ascites, œdema of feet, icterus; four last pregnancies ending in abortion.	Only one ostium of hepatic veins into vena cava present, and that admitted only a small probe and had thickened edges; firm adhesions of liver posteriorly at site of vena cava and also to diaphragm; nutmeg liver, enlarged, tough; spleen large; ascites; left hydrosalpinx.	Hepatic veins contained thrombi, some recent, others partly organized; portal-vein branches were "full;" liver cells degenerated, and in part necrotic; also an increase of connective tissue.	The stenosis of the hepatic veins appears to have been caused by an inflammation of the capsule and of the tissue at posterior surface of liver; the veins becoming stenosed by the dragging of the adhesions: possibly the process was of syphilitic origin.
Chiari (1) v. Maschka, 1899	28 years ♂	Previously always well; twelve days previous to death abdominal pain, and for the last fourteen hours continuous vomiting so that poisoning was suspected; delivered of healthy child five months previous to death.	The hepatic veins from their ostia to the smallest branches were filled with red and gray thrombi; their walls in the neighborhood of the vena cava showed circumscribed thickening; they admitted only the finest probe; liver was very large, surface smooth; spleen large; ascites; scar on under surface of labia major.	The walls of the hepatic veins were thickened throughout, the proximal parts showing marked inflammatory changes and a proliferating endo- and periphlebitis, extending a short distance along the vena cava; near the ostia, the endophlebitis caused stenosis by projecting elevations of newly formed tissue; liver congested, no increase of connective tissue.	Primary chronic inflammation of the proximal ends of the hepatic veins, probably syphilitic in origin.

Case.	Age and sex.	Clinical data.	Autopsy.	Microscopic data.	Conclusions of the author.
Chiari (2), 1899	55 years ♂	Woman had six children; five died in early youth; ill four weeks; ascites; œdema of legs, enlarged liver; sudden collapse.	The main trunks of hepatic veins entirely closed off by scar tissue from the vena cava, merely very small ostia being present; they contained thrombi, as did branches of portal vein; liver enlarged, capsule not thickened; spleen enlarged; hemorrhagic ascites and hemorrhagic infiltration of large intestine; partial aneurysm of left ventricle, obliteration of left coronary artery.	The ostia of the main trunks of the hepatic veins showed a proliferating endophlebitis: the vena cava showed near the openings slight thickening of the intima and in places adherent thrombi; the portal veins contained thrombi; the liver showed congestion and slight increase of connective tissue.	Primary obliterating inflammation of hepatic veins of long standing, the recent thrombosis causing the acute onset of symptoms, probably syphilitic in origin, for which the changes in the heart and coronary artery speak.
Chiari (3), 1899	29 years ♀	Abdominal pain, ascites, enlarged liver and spleen; death two months after onset; history of gonorrhœa.	Hepatic veins stenosed by thickening of their walls so that merely a probe could be inserted; the obstruction was increased by thrombi at the ostia; the liver enlarged, capsule somewhat thickened, cut surface showing a larger dark red area corresponding to diseased veins, and a smaller yellowish-brown area wherein the veins were merely slightly dilated; the branches of portal vein were dilated, but not thrombosed; spleen showed chronic enlargement; ascites; hyperæmia of stomach and intestines; hydrothorax.	The hepatic veins in their proximal and peripheral parts showed proliferating endophlebitis with thrombus formation, causing stenosis or complete obliteration; the portal veins were slightly dilated; the liver tissue in the dark area showed atrophy due to stasis, with slight increase of connective tissue and extravasation of blood; in the lighter areas, stasis was not present.	Primary endophlebitis of hepatic veins in the proximal and peripheral parts; secondary hepatic thrombosis with symptoms of stasis; possibly syphilitic in origin.
Churton, 1899	26 years ♀	Two years' history of enlargement of abdomen, and later distention of the superficial abdominal veins; not seriously ill until week before death; abdominal paracentesis showed blood-tinged fluid; history of trauma on right side previous to enlargement of abdomen.	The hepatic veins contained thrombi; one vein stenosed at entrance to vena cava contained an adherent thrombus, so that the ostium was difficult to find.	Hepatic veins obstructed by thrombi united to vessel wall by connective tissue; cirrhosis of liver with formation of "new bile-ducts."	Inclines to congenital syphilis as cause of stenosis of the hepatic veins and of cirrhosis of liver because no etiological factor could be found, and on the strength of successful mercurial treatment of a similar case.
Lazarus-Barlow, 1899	13 years ♀	Four months previous to exitus noticed swelling of abdomen, later melæna and hæmatemesis; on examination, superficial abdominal veins found distended, liver enlarged,	An hepatic vein was occluded by a mass of cicatricial tissue on the upper surface of liver posteriorly; the ostia were normal; the tissue extended 1½ inches into liver parenchyma, trabeculæ running from it into liver; the mass suggested a former gumma; numerous	Fibrosis of liver.	The hepatic veins obstructed by a cicatricial mass probably syphilitic in character; the thrombosis of the veins was secondary to the obstruction.

		icterus present; tapped twice, sinking after second paracentesis.	branches of hepatic vein occluded by partially adherent thrombi; a localized suppurative peritonitis was present.		
Thran, 1899	32 years ♂	Two weeks previous to illness, gave birth to a child which died when three weeks old; complained of abdominal pain and enlargement; laparotomy for ovarian tumor revealed ascites and enlarged liver; later œdema of feet; four paracenteses performed.	Hepatic veins containing adherent thrombi; nothing said as to state of ostia; adherent thrombus 1½ cm. wide in inferior vena cava at diaphragmatic opening; liver small with greatly thickened capsule which sent broad connective-tissue bands into parenchyma; spleen much enlarged with thickened capsule; chronic parietal peritonitis.	Hepatic veins thickened, to a marked degree in parts, especially in inferior of liver: they also showed inflammatory infiltration, and almost all contained thrombi; from these veins connective-tissue strands could be traced to the liver capsule; these, however, not following the veins, but being irregularly distributed; liver extensively destroyed by growth of fibrous bands; portal veins not thrombosed.	The obstruction of the hepatic veins due to the pressure of the fibrous bands which resulted from the perihepatitis; the perihepatitis is thought secondary to a peritonitis probably gonorrhœal in origin.
Kretz, 1900	48 years ♂	Ascites for half-year previous to death; exploratory laparotomy revealed adhesions about gall-bladder and thickening of parietal peritoneum in bands; death three months later from marasmus.	Ostia of hepatic veins stenosed or obliterated by white endothelial masses, only four remaining intact; portal vein not affected; left lobe of liver small; right lobe large: the Spigelian lobe, projected almost like a tumor, was congested, and contained the normal hepatic veins running to vena cava.	Microscopic picture said to correspond to first of Chiari's published cases.	Thinks stenosis and obliteration of hepatic veins is due to exuberant scar tissue at the ostia of the hepatic veins, formed as result of trauma; frequently result of coughing; a second cause is diminished coagulability of blood in the hepatic veins; a third, the possible presence of infl'matory elements in the blood, as in syphilis or in infectious diseases.
Lichtenstern, 1900	20 years ♀	Since youth frequent attacks of diarrhœa and abdominal pain; a year previous œdema of feet; admitted twenty-three days previous to exitus, showing slight icterus, ascites, pain in epigastrium and loins; later œdema of feet and trunk, bloody urine passed, and toward end slight hæmoptysis.	The ostia of the two main hepatic veins and smaller upper veins obliterated, small ostia seen below, including those of veins going to Spigelian lobe; the obstructed veins contained adherent thrombi; portal veins normal; vena cava showed areas of thickening, and contained soft parietal thrombi; liver of normal size, capsule normal, contained red and yellow areas, the latter especially in region of portal trunk and in Spigelian lobe; ascites; spleen normal; hemorrhagic erosions of stomach; rectal hemorrhoids.	Hepatic veins obstructed by connective tissue at ostia; peripherally endo- and periphlebitis and organized thrombi; portal veins normal; vena cava showed signs of chronic inflammation; liver in red areas showed atrophy due to congestion and increase of connective tissue; in yellow areas cells were well preserved.	Hepatic veins closed by a primary inflammation of their walls leading to a seconday thrombosis; congenital syphilis probably the cause, although no other lesion of syphilis found.
Rendu et Poulin, 1901	35 years ♂	Abdominal pain and distention, ascites, dilated abdominal veins; death 3½ months after first symptoms; diagnosticat'd as cirrhosis of liver with thrombosis of vena cava.	Nothing said as to state of ostia of hepatic veins; vena cava and portal veins normal; liver somewhat enlarged, slight perihepatitis, marked cyanosis; great development of Spigelian lobe; spleen enlarged and indurated; thickening of peritoneum.	Marked congestion of liver with atrophy about the hepatic veins; hepatic veins showed obliterating endophlebitis and thrombosis.	Believes the phlebitis of hepatic veins due to alcoholism, but not sure whether it was primary or secondary to the thrombosis.

Case.	Age and sex.	Clinical data.	Autopsy.	Microscopic data.	Conclusions of the author.
Penkert, 1902	22 mos. ♀	Ascites, caput medusæ, enlarged liver and spleen; marked constipation.	Hepatic veins obliterated at ostia, slight retractions of wall of vena cava being present; the veins peripherally dilated and thrombosed; portal vein narrow, otherwise normal; liver enlarged, congested; capsule normal; anastomotic venous circulation.	Walls of hepatic vein thickened; liver congested, connective tissue increased, new formation and widening of biliary canals.	Obliteration of hepatic veins probably congenital; nothing pointing to syphilis.
Moore, 1902	25 years ♂	Ailing for three years; continuous pain in hepatic area for one month prior to admission; abdominal swelling noticed three days previous, also œdema of feet; dilated lower abdominal veins present; liver not palpable; no jaundice; eruption on legs suspicious of syphilis; paracentesis, followed by death five days later; ill five weeks in all.	Right and left hepatic veins only marked by shallow dimples and absolutely impervious for about one inch from ostia; they contained thrombi; liver small; no perihepatitis; it showed advanced central red atrophy; spleen small, congested; ascites; ductus venosus closed.	Hepatic veins closed by sparsely cellular connective tissue; media distinct, but showing intercellular fibrosis; intima thickened and obliterating the lumen; adventitia normal; hepatic veins thrombosed; liver showed central red atrophy, congestion, and hemorrhage.	Primary cause of obliteration of veins was endophlebitis, possibly due to syphilis; its localization to this area possibly due to the susceptibility of the veins in the vicinity of the ductus venosus to further obliteration.
Fabris, 1904	16 years ♀	Hemorrhagic ascites two months before death.	Large ostia of hepatic veins closed, only smallest existing; recent and older thrombi in hepatic veins; the vena cava somewhat whiter at site of obliterated openings; liver small, no perihepatitis; consistency increased; cut surface showed red zones and yellow zones. Caput medusæ.	No signs of proliferating endophlebitis of hepatic veins or of vena cava; walls normal; liver congested, with increase of bileducts.	Believes obliteration to be of congenital origin, as no reason to presuppose syphilis, and impossible to imagine an inflammation not leaving more evidence.
Meystre, 1904	28 years ♂	Three weeks previous to admision to the hospital complained of abdominal swelling; ascites found; operation, from which patient died two and a half months after onset of symptoms.	Hepatic veins contained thrombi; some were changed into connective-tissue bands, some showed thickened walls; the vena cava showed adherent thrombi overlying the obliterated ostia of the hepatic veins; some hepatic veins were patent; portal vein normal; liver congested and large; spleen enlarged; ascites.	Hepatic veins contained thrombi; some showed a thickened wall, the lining being irregular; in others the lumen was replaced by connective tissue; the vena cava inferior showed thickening of the intima at site of ostia of hepatic veins; portal veins normal; liver markedly congested, showed atrophy of parenchyma, combined with hypertrophy of some liver cells.	Primary endophlebitis of hepatic veins; no etiological factor present; author however inclines to syphilis as the cause.

An examination of the above columns shows that males and females have been affected in about equal numbers. Time of life brings with it no marked predisposition, as the ages of the patients have varied from seventeen months to fifty-five years, including the intervening decades; however, only three patients were over forty years of age. When we consider the clinical data, we find a general conformity in the course of the disease. The onset is generally gradual. Abdominal pain or discomfort, often most marked in the hepatic region, or an increase in the size of the abdomen, is almost invariably the first symptom, although for weeks or even months it may not be severe enough to cause the patient to seek medical advice. In some instances gastric symptoms have occurred later, but in a large majority these were not recorded. On examination the enlargement of the abdomen was found to be due to ascites, which rapidly increased and necessitated repeated paracenteses at short intervals. The fluid withdrawn had the characteristics of a transudate, but in 2 cases was slightly hemorrhagic. A caput medusæ, or distended abdominal vein, was often present. Œdema of the feet and anasarca occurred as late manifestations. Icterus was rarely noted, and then only of slight grade. The liver was invariably found enlarged, firm, and smooth in the early stage, but later small and slightly nodular. The spleen was large and firm. Temperature normal. Urine negative. The course of the disease rarely extended beyond six months from the date of onset. Such is the general clinical picture drawn from the 23 cases reviewed. The most marked variation from this type was the case of Lichtenstern, characterized by sudden onset and by gastric symptoms, resembling acute poisoning, followed by death within twelve days. When we review the conclusions, we find the greatest differences of opinion among the various authors. Most of them are in doubt, but each suggests a probable cause. Here, again, I believe, a table will most clearly show what these different opinions are:

	Perihepatitis.	Hepatitis.	Thrombosis.	Primary phlebitis.	Trauma.	Congenital anomaly.
Frerichs	2					
Rosenblatt	...	1				
Gee	...	1				
Schüppel	...	...	1			
Hainski	1					
Lange	...	...	...	1		
Kelynack	1					
Chiari	...	...	...	3		
Churton	...	...	...	1		
Lazarus-Barlow	...	1				
Thran	1					
Kretz	...	...	...	...	1	
Lichtenstern	...	...	...	1		
Rendu and Poulain	...	...	...	1		
Penkert	...	...	...	...	...	1
Moore	...	...	...	1		
Fabris	...	...	...	...	...	1
Meystre	...	...	...	1		
	5	3	1	9	1	2

A glance at the above table will be sufficient to show how varied are the views as to the cause of the disease. I shall not discuss the question of etiology at this point, but shall proceed to the consideration of the case which came under my personal observation.

The patient was a girl, aged sixteen years, in the general hospital at Prague, on the service of Professor Pribram, to whom I am indebted for the careful history. Family history negative; no indications of syphilis. Had always been pale and weakly, and had never menstruated. Had had none of the diseases of childhood. Four years previously she had been a patient in another division of the hospital, suffering from marked abdominal distention, causing dyspnœa. She remained there for six months, during which time the ascites gradually disappeared under diuretic treatment and after frequent paracenteses. She was discharged, with the diagnosis of hypertrophic cirrhosis of the liver. From that time until October 1, 1904, had performed light housework at home. She then began to suffer abdominal pain, without apparent cause, and within three days experienced marked swelling of the abdomen and distention of the veins of the upper abdominal wall. Although she left perfectly well otherwise, these symptoms induced her to apply for admission to the hospital. The results of the physical examination may be summarized as follows:

Face pale, lips and extremities cyanotic. Clubbing of toes and fingers. The veins of the thoracic wall appeared like a meshwork, from the midst of which a markedly distended vein extended toward the abdomen. The heart showed great pulsation and dilatation to the right; sounds muffled, pulse soft and rhythmic. Lungs negative, abdomen distended, the maximum circumference being 87 cm. The vein extending upon the abdomen from the thorax contained tender nodules. Movable fluid, extending to within 2 cm. of the umbilicus, could be clearly distinguished. Liver was palpable 2 cm. below free border of ribs, consistency firm, surface somewhat nodular. Spleen extended 1 cm. below free border of ribs. Inguinal glands not enlarged. External genitals infantile. Lower extremities not œdematous.

October 29th. Circumference of abdomen 89 cm. Diarrhœa.

31*st.* Abdominal pain. Sleeplessness. Diarrhœa. Afternoon temperature yesterday, 100.8°. Abdominal paracentesis with removal of 6 litres of slightly cloudy yellow fluid. The liver palpable three fingers below free border of ribs, hard, surface granular.

November 1*st.* Abdominal circumference 67 cm.

6*th.* Abdominal circumference 76 cm. Distention of veins includes upper abdomen, whereas yesterday it was confined to thorax.

7*th.* Abdominal circumference 78.8 cm.

8*th.* Abdominal circumference 79 cm. No œdema of feet.

9*th.* Severe abdominal pain.

13*th.* Death.

During her stay in the hospital the patient frequently had temperature as high as 100.8°. The urine was diminished in quantity and contained traces of albumin. The pulse tension (Gärtner) varied between 65 and 100. The treatment consisted in urea, theocin, and lecithin, at various periods, but all without effect.

Diagnosis. Cirrhosis hepatis and chronic peritonitis.

An autopsy was performed by Professor Chiari the day after exitus. The following is an abstract of the protocol: Body emaciated. Tonsils and cervical lymph nodes somewhat enlarged. Abdomen markedly distended; fluctuation present. The external genitalia were undeveloped and showed several superficial, firm, scars. From the mons veneris a bridge of skin, 3 cm. in length, stretched so as to form a furrow, extended to the clitoris. On opening the abdomen, greatly dilated subcutaneous and subperitoneal veins were apparent in the umbilical and in the epigastric areas. These ectatic veins were most numerous along the round ligament of the liver. Lungs adherent over entire surface; congested, slightly œdematous. Peribronchial nodes not enlarged. Pericardium contained 2 drachms of clear serum. Heart somewhat enlarged; the myocardium of light-brown color. Œsophagus dark red; its lower half showed markedly dilated submucous veins. The abdomen contained about 6 litres of clear serum. The peritoneum slightly thickened, smooth, glistening, especially thick over liver and spleen. Over the former it was "Zuckergussartig," or "iced," in patches. The omentum to a considerable extent adherent to the anterior abdominal wall in the epigastric area. It contained many dilated veins. Liver very small. Its width 20 cm., length 11 cm., thickness at point of greatest depth 7 cm.; its weight 950 gm. The surface showed numerous nodes, some 1 cm. in diameter. Consistency firm and tough. The cut surface of the liver showed everywhere numerous light-brown, circumscribed nodules, as large as a bean, projecting slightly from the surrounding parenchyma, which was grayish and of firmer consistency. No patent branches of the hepatic veins were apparent near the vena cava, but, instead, what seemed to be obliterated veins. The branches of the portal vein were patent throughout. The bile-ducts contained very dark bile. The trunk and main branches of the portal vein were dilated. The umbilical vein was present and patent for an ordinary anatomical sound. The intrahepatic portion of the vena cava was remarkable in that no ostia of the hepatic veins were visible on its inner surface. Ductus venosus arantii completely obliterated. Spleen weighed 170 gm., slightly enlarged. On section, tough, moderately vascular, trabeculæ soft. Malpighian corpuscles not evident to the naked eye. Kidneys moderately vascular, surface smooth, capsule non-adherent. In the perirenal tissue of the left side very numerous dilated veins, which could be traced into the mesentery

of the descending colon. Mucosa of urinary bladder somewhat œdematous. Accessory ovaries present on both sides. Stomach contained stringy mucus; mucous membrane pale.

The middle third of the small intestine was intensely red, its wall greatly swollen by hemorrhagic infiltration, and nearly 1 cm. in thickness. This part as well as the adjacent lumen contained much fluid blood. The veins of the mesentery of this section were dilated and contained obstructing thrombi, which were reddish and friable. The arteries were normal. The splenic vein contained fluid blood. The mucosa of large intestine was slightly reddened. Pancreas and adrenals were pale.

The pathologico-anatomical diagnosis was: Obliteration of the hepatic veins at the ostia in the inferior vena cava. Obstruction of the hepatic veins in the liver. Atrophy of the liver. Dilatation of the submucous veins in the lower part of the œsophagus, of the subperitoneal veins, of the subcutaneous veins at the umbilicus, with persistence of the umbilical vein. Adhesion of the omentum to the anterior abdominal wall in the epigastric region, and dilatation of its veins. Hydrops ascites. Thrombosis of the mesenteric veins with hemorrhagic infiltration of part of the small intestine. Accessory ovaries. Scars of external genitals. Abnormality of vulva.

Before detailing the result of the microscopic examination, I wish to describe more fully the macroscopic picture of the liver and the hepatic portion of the vena cava. The conformation of the liver and the appearance of its cut surfaces were striking. Two points were noticeable at a glance: the relative smallness of the left lobe and the relative greatness of the Spigelian lobe, which, viewed from the posterior surface of the liver, projected downward like a tumor mass from the body of the organ. This abnormal development of the Spigelian lobe must not be looked upon as an accidental condition, as several of the reported cases showed a similar local development. It is to be considered, in a measure, characteristic. Closer examination of the various cut surfaces of the liver showed that the light-brown or yellowish nodules mentioned in the protocol were distributed throughout the organ and that they varied in size from a pinhead to 2.5 cm.; that they were not more numerous in the large right than in the small left lobe; that they were round or oval in shape, and were almost invariably surrounded by a definite ring of firmer tissue, macroscopically suggesting connective tissue. We next followed and examined the hepatic veins, the inferior vena cava, and the branches of the portal veins as they appeared successively in the various horizontally cut segments of the liver. The obliterated hepatic veins could without difficulty be traced into the parenchyma, in some segments for 2 to 3 cm., extending from the vena cava as firm, gray bands, without lumen. The vena cava in the posterior surface of the liver showed four minute ostia, ranging

from a pinpoint to a pinhead in size. Three were at the upper angles of the vena cava, one to the left, two to the right, at the sites of the two main hepatic veins; the fourth was situated to the right of the median line at about the centre. The vena cava itself showed no stenosis. The portal vein likewise showed changes to the naked eye. Its right branch was obstructed by firm-contracting tissue not far from the porta hepatis; its left branch contained fresh thrombi, surrounded by reddish liver parenchyma.

The entire hepatic portion of the vena cava with the underlying liver tissue was removed for microscopic examination. Seven segments were thus obtained. Portions of the interior of the liver as well as of the spleen were also excised. All were hardened in alcohol and embedded in celloidin. Section after section was cut in order to follow an hepatic vein to its outlet, and to show the obliterated vessel in continuity with the vena cava. The Van Gieson and the hæmatoxylin and eosin stains were employed. However, a rapid examination of the unstained specimen often sufficed to show that the ostium of the vein had not been encountered. The obliteration was in all cases caused by connective tissue at the ostia, which was continuous with that of the intima of the vena cava. Up to this point the veins were to some extent patent. The obliterating connective tissue was dense, slightly cellular, and in parts contained lacunæ filled with blood. Careful search could not reveal any pigment therein, such as one should expect to find if the obliterating connective tissue had replaced a primary thrombus. The stenosis which existed in all cases beyond the point of obliteration was due to a proliferation of the intima. Here a thrombus was frequently found blocking the lumen. The media of the veins was well preserved, and ran in an uninterrupted course with that of the vena cava. Nowhere was a break therein to be seen as if trauma had caused a previous rupture of the fibres. The adventitia was also normal. The vena cava often showed a marked depression at the site of some obstructed ostia. Near these sites the connective tissue of its intima was thickened. At one point a partly organized thrombus was attached, but beneath it the connective tissue of the intima continued unbroken.

The liver parenchyma showed dilatation of the central veins, with atrophy of the liver cells in the centre of the lobules. There was a marked increase of connective tissue, which ran in bands through the parenchyma. Bile-ducts were numerous. The yellowish nodules, so striking in the macroscopic picture, proved to be composed of cells in a good state of preservation, showing no atrophy. They stained less deeply with eosin; but the nuclei took the hæmatoxylin well and were of average size. These areas were distinctive in showing no dilatation of the capillaries, a small rather than a large number of bile-ducts, and no increase of connective tissue. The spleen showed moderate congestion, but was otherwise normal.

From a clinical and a pathological standpoint this case is fairly typical. It must be regarded as one of long standing, having lasted at least four years. I consider that the patient was already suffering from an hepatic endophlebitis when in the hospital for the first time, although her disease was at the time diagnosed as hypertrophic cirrhosis. Later she improved, and the ascites remained away for the long period of four years, probably as the result of the compensatory circulation, which, as the autopsy showed, had established itself. The endophlebitis, however, continued, causing the stenosis of the ostia to become more and more marked, until finally obliteration occurred. This absolute closure of the hepatic veins, and barrier to the outflow of the large volume of venous blood from the liver, was the beginning of the end, and led to the sudden and persistent ascites which drained the strength of the patient.

The pathological findings serve to justify this interpretation. That we have to do with a case of long standing is borne out by the cirrhotic-like, granular liver, by the dense connective tissue obliterating its veins, and by the yellowish areas scattered throughout the parenchyma, which I look upon as regenerative areas, or so-called liver adenomata.

What cause can be assigned for this obliteration of the venous circulation, so strangely localized in one small area? No hereditary constitutional taint was disclosed; no previous illness of the patient existed upon which to cast the blame. Even the autopsy revealed little besides the venous obliteration and its immediate consequences upon the liver and the portal system. I believe that an obstruction of the hepatic veins can most certainly be caused by a perihepatitis, as happened in the cases reported by Frerichs[3] and others. But no such condition was found to explain this case. A primary thrombosis of the ostia I could not assume, partly because there was no reason for the formation of multiple thrombi in healthy veins, but still more because, as I mentioned above, no vestiges of a clot, no pigment, could be found at the site of obliteration. I have no doubt, however, that thrombosis also may be the primary cause of an obliteration through the formation of connective tissue. It has been urged by Kretz[20] that all these cases are due to trauma, to tearing of the hepatic veins, which are to be considered as constituting the insertion of the liver to the inferior vena cava; that small tears are brought about by coughing, and result in an exuberant scarring of the vessel wall, diminished coagulability of the blood in the hepatic veins, preventing thrombus formation. An argument of this nature cannot be discussed theoretically; everyone is entitled to his individual opinion as to the probable occurrence of such minute traumatic lesions. However, Kretz also bases his opinion upon the fact that microscopically he has seen a deflection and irregularity of the media of the obliterated veins at their insertion

into the vena cava. With this point in view I examined the muscular coat of the veins most carefully, but could nowhere find a break in the media. In every instance I could follow it unbroken and undeflected into that of the vena cava. For this reason I cannot accept a traumatic origin for my case and must look for another cause. The etiological table given above shows that two cases have been ascribed to a congenital closure of the hepatic veins. To grant this as the etiological moment we should have to conclude that such a lesion might exist without symptoms for twelve years, or, if we apply it to many of the other published cases, well on into middle life. But what I believe furnishes absolute evidence against this origin is that the ductus venosus arantii was not patent. As Lazarus-Barlow[12] well says, this would not become obliterated under such abnormal conditions. Moore[19] and Rolleston[23] modify the congenital point of view by suggesting "a spread of the process of obliteration of the ductus venosus to the hepatic vein orifices—an excess of the obliterating process." This might well be true for the obliteration of the ostium of the left main hepatic vein, or for the vena cava at this point, but a study of the anatomical relations of this region does not allow me to believe that all the large hepatic ostia could be obliterated without causing some stenosis of the vena cava itself.

All the cases which I have considered above, as well as the one just reported have been uncomplicated by any narrowing of the hepatic vena cava. I now come to the last cause to be considered: a chronic endophlebitis. Clinically, my case and the majority of the cases, were slowly progressive in character. Pathologically, such change was found as is generally ascribed to chronic inflammation; a proliferation of dense connective tissue such as blocked the obliterated veins. Of all the causes advanced this one seems the most probable. We cannot, however, pronounce this view absolutely; as we are unable to define the exciting inflammatory cause. All but one of the writers who believe an inflammation to be the basis of the disease ascribe the changes to syphilis. However, to whichever opinion we incline, we must not lose sight of the fact that a close study of the cases shows that, with the exception of Chiari's first and, possibly, second case, none showed any other definite syphilitic lesions. If syphilis be regarded as one cause of the inflammation, it is probable that it is not the only one, but that inflammatory toxins of other natures can produce a like effect upon the lining of the hepatic veins.

As regards the diagnosis, I believe that I can venture the statement that no case of this disease has been correctly diagnosed. The cases have generally been confused with cirrhosis of the liver, although the ascites has also led to the diagnosis of tuberculosis or carcinoma of the peritoneum, and even to that of ovarian cyst. The two fulminating cases, characterized by vomiting, prostration,

and a rapid course, were diagnosed as due to poisoning in the one instance and to intestinal obstruction in the other. It would lead to nothing to consider these cases further, as, in the present state of our knowledge, we could not hope to suspect the underlying condition when presenting itself in this violent form. But a study of the other cases shows that although this disease cannot be absolutely diagnosed, it can and should be thought of when a certain group of symptoms presents itself.

We have the typical signs of cirrhosis of the liver: ascites with dilated abdominal veins, sometimes a caput medusæ, very slight or no icterus, a palpable liver in the early stages, and a palpable spleen. What can lead us to suspect an obliteration of the hepatic veins as the cause? In the first place the history of the patient; the absence of all etiological cause for a cirrhosis. This is important. If, in addition to this, the patient is a very young individual, as is often the case, our suspicion should be awakened to the possibility that we are not dealing with an ordinary cirrhosis, a disease of late middle life.

Furthermore, an important differential diagnostic point is the occurrence of pain over the hepatic area, or localized in the upper abdomen, which is one of the most constant and earliest symptoms of endophlebitis, but exceptional in cirrhosis. Again, as Quincke[14] says, the rapidity with which the swelling of the liver and ascites develop is of importance. The patient with chronic endophlebitis will generally state that the swelling of the abdomen has showed itself within a few weeks or even a few days. In striking contrast to this is the gradual onset of abdominal swelling and ascites in cirrhosis. Later in the course of the disease the rapidity with which the ascitic fluid collects, the frequent necessity of paracentesis, point to an essentially obstructive lesion. All these symptoms, however, although brought about by a disease of the hepatic veins, are directly dependent upon the secondary obstruction in the portal system and are typical of portal obstruction. We cannot distinguish between them, and it is only the lack of cause for a portal obstruction that should make us consider whether this condition is not the result of a primary hepatic obliteration.

Beyond this we cannot go in the differential diagnosis. The paucity of cases presented for review does not allow of greater generalization. I am certain, however, that if this disease is taken into consideration at the bedside, and looked for in the postmortem room, we shall before long find many more upon which to base an opinion. Again, I wish to lay stress on the importance of opening the hepatic portion of the vena cava, and examining the ostia of the hepatic veins in all cases, but especially in those where ascites has been present.

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A CASE OF EXCISION OF THE HEAD OF THE HUMERUS FOR CONGENITAL SUBACROMIAL DISLOCATION OF THE HUMERUS.[1]

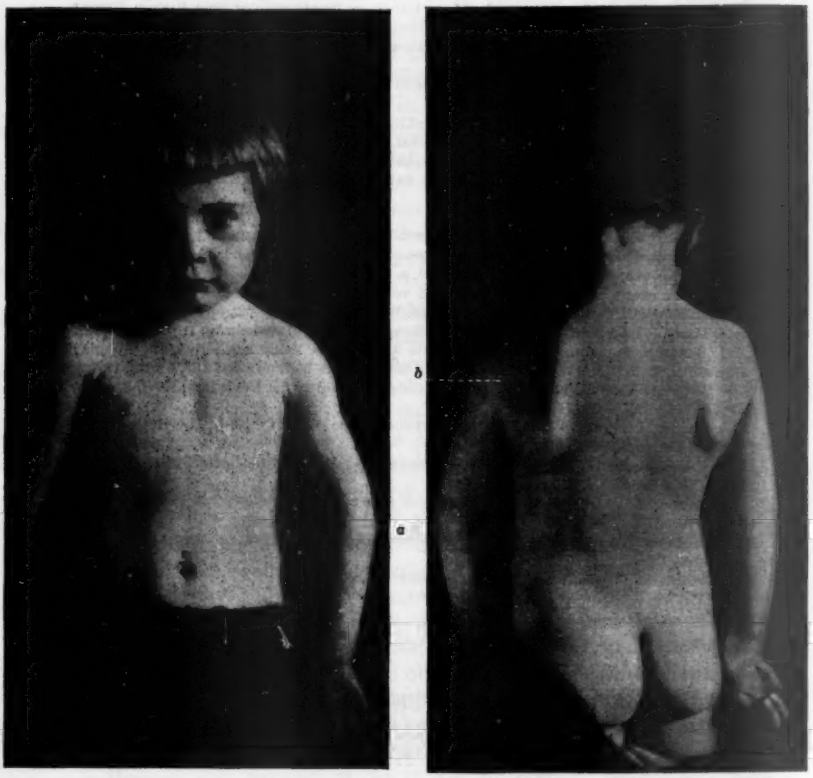
BY JOHN B. ROBERTS, M.D.,
OF PHILADELPHIA.

A BOY, aged three years, was operated upon on December 5, 1903. The head of the bone could be seen and felt under the acromial process, and the humerus was firmly abducted from the chest with the external condyle pointing almost directly forward instead of

[1] Read by title at the meeting of the American Surgical Association, July 5, 1905.

outward. The position of the arm and attached forearm was due to the rotation of the humerus, caused by the displacement of the head of the bone. Voluntary elevation of the arm was impossible and other movements were restricted. It was, therefore, deemed advisable to attempt replacement of the head of the bone by opera-

FIG. 1 FIG. 2



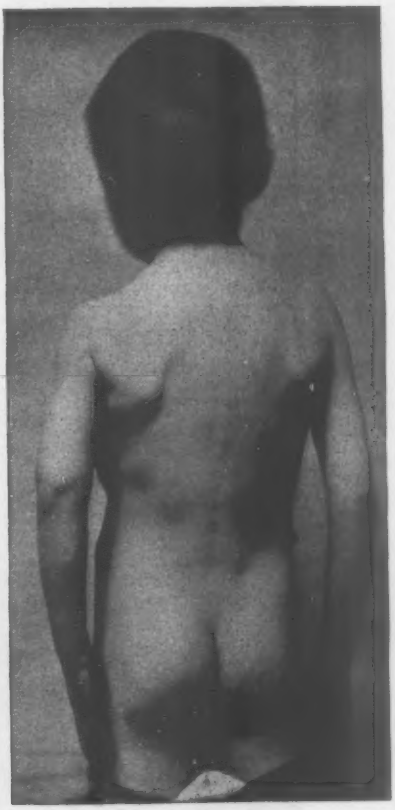
Congenital subacromial dislocation of the left humerus. Boy, aged three years. Observe abduction and inward rotation of humerus. Before operation. a. Olecranon points directly outward and external condyle forward. b. Head of humerus.

tion, and in case of failure, to excise the humeral head. A vertical incision, three inches long, was made over the prominence below the acromion, through the fibres of the deltoid. The round head of the bone was covered by a deeper muscle, which was probably the infraspinate. After opening the capsule and exposing the head, attempts were made to reduce the dislocation. As reduction was

impossible, an incision about three inches long was made in a vertical direction through the deltoid on the front of the shoulder and carried down to the deep layers of muscle. Counterpressure upon the bone was made here in the endeavor to aid in the reduction of

FIG. 3

FIG. 4



Congenital subacromial dislocation of left humerus. Same patient as Fig. 1. Photograph taken about eighteen months after excision of head of the humerus. Observe improved position of elbow, but the shortening of humerus. *a*. Body of biceps unnaturally prominent because origin of one head is lost.

the luxation. All these efforts were unavailing. The glenoid cavity itself was not exposed, because of the depth of the wound and the youth of the child. The condition seemed to make it evident that only a prolonged and bloody dissection would thoroughly expose

the glenoid cavity. I therefore came to the conclusion that excision of the head of the bone would give probably as good, if not a better, joint with less risk. Reduction with stiffness of the joint seemed to me to be but little better than the present condition. The head of

FIG. 5

Congenital subacromial dislocation of the left humerus. Same patient as Fig. 1. Observe abduction rotation of humerus, shown by the elbow being held away from the thorax, with olecranon pointing outward.

the bone was thoroughly exposed and excised through the posterior wound. The section was made with a small saw close to the head, so as to remove as little as possible of the shaft. In removing the excised fragment the long head of the biceps was divided in the

depth of the wound close to the axilla. The rotation of the bone caused the bicipital groove and its enclosed tendon to be almost directly opposite the incision made on the back of the joint. The

FIG. 6

Congenital subacromial dislocation of the left humerus. Same patient as Fig. 1. Skiagraph taken about three months after excision of the head of the humerus. Observe the absence of abnormal rotation of the humerus, which is seen in the skiagraph taken before operation. The abduction of the humerus seen here is voluntary.

division of this muscle was not recognized at the time. Both cuts were closed without drainage and the forearm supported by a sling. Union occurred by first intention.

When seen on March 2, 1904, the motion of the arm was good, though the limb was weak. The child had a tendency to aid it by lifting it with the right hand when told to raise it. He could touch the ear on both sides and the back of the head with the left hand if the arm is aided a little with his own right hand or an attendant's hand. This aid is needed especially when he touches the right ear. His mother said that he always helped the dislocated arm with the other hand, and that this habit was still kept up, though there was much less need of such assistance. Frictions and calisthenic exercises were recommended.

When examined June 1, 1905, the notes made were as follows: The left humerus is considerably shorter than the right. Passive motion elicits grating at the shoulder-joint. There is possible moderate rotation, though it is not as complete as on the right side. Elevation of the humerus is restricted, and the scapula moves with the humerus, if passive movements are at all extensive. There is still some rotation forward of the humerus when the arm is held at rest, so that the external condyle presents rather more forward than in the normal arm. The boy can now touch the back of his ear and neck on the left side. He can put his hand to his mouth, which he could not do before, and he can clasp his hands behind his back in the lumbar region. The normal arm from the acromion to the external condyle is six and one-half inches long. The left arm from the acromion to external condyle measures five and three-quarters inches. The belly of the biceps stands out prominently in the middle of the arm. This is due largely to the division of its long head at the operation. The forearm is somewhat atrophic, and the left hand seems slightly smaller.

He cannot lift the left hand over his head, but he can nearly touch the occipital region. He uses the right hand to lift the left arm when he desires to put the left hand on top of his head.

His general health is good and the scapular muscles seem about as well developed as on the other side. The deltoid seems to be a little more prominent than on the other side.

It is doubtful whether he can voluntarily bring the left elbow in contact with his ribs, but he can put the left hand on the right shoulder and bring the elbow and humerus close to the ribs. It is difficult to determine the exact amount of adduction, because of the youthfulness of the child and the difficulty of making him understand.

The deformity of which this case is an illustration is unusual. There has been considerable discussion as to how many of such cases are traumatic dislocations caused by injuries at the time of delivery. I see no reason to doubt that a large proportion of them are the result of intrauterine conditions. Accidental subspinous or subacromial luxations are so rare in both adults and children that it seems to me reasonable to look upon them, when found immediately

after birth, as true congenital conditions. It is true that violence during delivery may cause the lesion, and also that such displacements may be the result of a muscular paralysis occurring before birth or during delivery. It is quite possible, therefore, that some of the cases reported belong to these groups. The occurrence of this posterior displacement occasionally in both shoulders of the same infant and at times in more than one child of the same family is strong evidence, in my opinion, of the prenatal origin of the bony abnormality. I have not been able to find many cases recorded in the literature which bear rigid analysis. Stimson[1] says that he has seen 4 or possibly 5 cases. Phelps had seen, according to Stimson, 6 or 7. Scudder[2] reports 2; Küster,[3] 1 bilateral case; Gaillard,[4] 1; R. W. Smith,[5] 1 bilateral case; Cumston,[6] 1; Peckham,[7] 2; and I reported a previous case ten years ago to this Association.

VOLVULUS OF THE CÆCUM AND ASCENDING COLON.

By Alfred C. Wood, M.D.,
of Philadelphia,
Assistant Professor of Surgery, University of Pennsylvania; Surgeon to the University, Philadelphia, and St. Timothy's Hospitals.

Mrs. O. B., aged thirty-four years, widow (Philadelphia Hospital, No. 1756), was admitted from the out-wards on account of severe abdominal pain and vomiting, September 14, 1903.

Her statement was as follows: On the evening of September 13, 1903, she lifted a heavy woman into bed, and afterward "felt badly," although she did not report the matter and did not do anything to get relief. About 11 o'clock on the following morning she felt a sudden, very sharp, lancinating pain in the abdomen. The pain continued, was paroxysmal in character, and was so severe as to cause her to cry out; it seemed distributed equally over the abdomen. Vomiting began soon after the pain, and has since been almost continuous. The bowels acted regularly and normally until the

[1] Fractures and Dislocations, ed. 1905, p. 606.

[2] Archives of Pediatrics, 1890, vii. p. 260.

[3] Ein Chirurgisches Triennium, 1882, p. 256; also in Berlin. klin. Woch., January 6, 1879, Bd. i. p. 9.

[4] Mém. de l'acad. de méd., 1841, p. 703; quoted fully by Alph. Robert in Des vices congénitaux de conformation des articulations, Paris, 1851, p. 53.

[5] An Essay upon the Original or Congenital Luxations of the Upper Extremity of the Humerus, Dublin Medical Journal, 1839, vol. xv. p. 249; also mentions the case in his Treatise on Fractures, Dublin, 1854, p. 256.

[6] The American Journal of the Medical Sciences, June, 1903.

[7] American Journal of Orthopedic Surgery, April, 1905, p. 386.

beginning of the present trouble, two days ago, since which time there has been no movement. The menstrual function is normal, the last period having been two weeks prior to this attack. The patient has one child living and in good health. There have been no miscarriages. There is no venereal history.

Physical Examination. The patient looks older than the age she gives. She is well developed and fairly well nourished, the face is pale, and the expression denotes acute suffering. The tongue is moist and clean. The pupils are small, equal, and contract normally. The lungs are normal. The heart sounds are regular, but weak; pulse 86 and compressible. The abdomen is much distended, apparently more on the left side than the right. The surface above the umbilicus is red from the effects of a mustard plaster; striæ gravidarum are prominent. The abdomen is everywhere board-like to the touch, no definite mass can be felt, and palpation gives the patient severe pain. The abdominal pain is reflected up to the region of the right shoulder. Flexing the thighs upon the abdomen gives marked relief. During the severe pains the patient groans and tosses about the bed.

Nausea and vomiting are almost constant. The vomitus is black, watery, and has a sour odor, but is not bilious or fecal. There is a great deal of retching. The skin is bathed in a cold perspiration. The leukocyte count is 26,400. The urine contains albumin and hyaline and granular casts.

Operation, September 15th. The writer did not have an opportunity of examining the patient until she had been placed under the influence of ether on the operating table. It was then possible to palpate a large, rounded, uniform mass, occupying chiefly the right lower quadrant of the abdomen. The abdomen was opened through an incision along the outer border of the right rectus muscle. A quantity of dark-colored, offensive fluid escaped from the abdominal cavity when the peritoneum was opened. Peritonitis had evidently already begun. The tumor was found to be a distended loop of intestine, which on inspection proved to be a volvulus. The bowel forming the volvulus was lustreless and of a deep purple color, looking almost gangrenous. There did not seem to be anything but gas in the distended loop. The bowel was delivered from the abdomen and untwisted without incising, the distention disappearing as reduction took place. The volvulus was composed of the cæcum and part of the ascending colon. Every portion of both of these structures was so devitalized that resection was imperative. The ileum adjacent to the cæcum appeared to be but little affected, there were no gross changes that would lead one to question its vitality. The latter was therefore divided near the ileocæcal valve and the colon at the hepatic flexure, the two ends being united without difficulty by means of Murphy's large-size button. The gauze pads which had surrounded the field of operation were

removed, the abdominal cavity was thoroughly flushed with sterile water, and the wound closed by interrupted sutures.

The operation was concluded about 5 P.M. At 7 o'clock the pulse was recorded as 84, temperature 99⅖°, respiration 28. There was but little change until 9 o'clock, when the pulse and respirations rose rather rapidly, and the temperature gradually. From this time on the patient failed steadily, and died at 4 o'clock the following afternoon, twenty-three hours after operation, the pulse having reached 180, the respiration 56, and the temperature 103⅗°.

The autopsy showed that several inches of the ileum adjacent to the point where it had been divided had become gangrenous, and there was a general peritonitis.

COMMENT. A careful study of the relations of the parts affected was impossible, on account of the necessity of concluding the operation as speedily as possible. The conditions found, however, appeared to be as follows: The cæcum was at the upper extremity of the tumor and internal to the colon. A single turn relieved the volvulus.

The mechanism of this case seems to have been as follows: first, the descent of a loop of ascending colon, made possible by an abnormally long mesocolon; the falling of the colon revolved the cæcum on its anteroposterior axis, so that it first pointed toward the right and, as the process continued, upward. As distention in the loop took place the cæcum was forced upward along the parietal wall, carrying the ileum with it, until it finally crossed over the ascending colon anteriorly.

Treves divides volvulus of the ascending colon and cæcum into three categories:

"1. A twist of the ascending colon around its own axis.

"2. Twists brought about by an abnormal loop formed by the ascending colon and cæcum with a long and distinct mesocolon.

"3. Twists of the cæcum 'upon itself' or about its own axis."

The case here reported belongs to the second division. According to Treves, more than two-thirds of all cases of volvulus of the intestine occur as a result of rotation of the sigmoid flexure on its mesenteric axis. The above case is of interest on account of its rarity. Treves states that twists of the cæcum and ascending colon are among the least common varieties of intestinal obstruction.

As to the causes of volvulus of the sigmoid, the same authority states that chronic constipation ranks first; while in the second and third of the varieties just mentioned some congenital abnormality has been present in all the reported cases, without which the twist could not have occurred. This abnormality related either to defective development of the cæcum—that is, to a faulty position—or to an unusually long mesentery.

Peritonitis is a very constant and early complication in these cases. When the loop of intestine is greatly distended the overlying peritoneum may be torn in one or more places. Such a rent is to be observed in the accompanying illustration:

Increased interest has been given to this subject by Corner and Sargent,[1] who publish an anaylsis of fifty-seven cases. They

[1] Annals of Surgery, January, 1905.

emphasize the point that while acute examples of this condition have been recognized for a long time, it does not seem to have been observed that subacute and chronic forms also occur. In illustration, the duration of the symptoms in the fifty-seven cases was as follows:

Less than 1 day	7 cases.
1 to 2 days	2 "
2 " 3 "	6 "
3 " 4 "	5 "
4 " 5 "	4 "
5 " 6 "	4 "
6 " 7 "	1 "
8 " 14 "	10 "
15 " 21 "	3 "
Unstated	10 "
Described as "chronic"	4 "

Moreover, the authors state a number of the patients had suffered premonitory attacks of abdominal pain and vomiting, the last attack differing only in degree from the previous ones.

Examination of the records shows that a considerable number gives accounts of previous and recurrent abdominal trouble, and even of definite intestinal obstruction, which have passed off. Such attacks vary in duration from a few minutes to several days. Some patients have been subject to them for months or years; while in other cases the premonitory attacks have preceded the final acute one by only a few weeks or days.

The most constant symptom is abdominal pain, which naturally varies greatly in character and intensity in different cases. The most frequent concomitants are vomiting and inaction of the bowels, as regards both flatus and feces. The abdomen may rapidly become distended; in some instances a resonant tumor may be recognized. As regards age, the cases were distributed as follows:

Under 5 years	3 cases.
5 to 10 "	1 "
10 " 20 "	7 "
20 " 30 "	15 "
30 " 40 "	14 "
40 " 50 "	7 "
50 " 60 "	4 "
60 " 70 "	2 "
70 " 80 "	1 "
Adult	1 "
Unstated	2 "

The extremes were 19 days and 80 years.

FURTHER OBSERVATIONS ON THE RELATION OF LESIONS OF THE GASSERIAN AND POSTERIOR ROOT GANGLIA TO HERPES OCCURRING IN PNEUMONIA AND CEREBROSPINAL MENINGITIS.[1]

By William Travis Howard, Jr., M.D.,
PROFESSOR OF PATHOLOGY, WESTERN RESERVE UNIVERSITY.

(From the Pathological Laboratory of the Lakeside Hospital, Cleveland, Ohio.)

Introduction. At the meeting of the Association in 1902 I reported two cases of herpes, one of the lip and nose and the other of the trunk, occurring in acute croupous pneumonia, in both of which the sensory ganglia supplying the areas affected with herpes showed acute degenerative and exudative changes.

At this time I suggested that careful examination would disclose similar lesions in the sensory ganglia supplying areas affected with herpes, complicating other infectious diseases, especially cerebrospinal meningitis, typhoid fever, and malaria.

Since then I have had opportunity to examine at autopsy two cases of cerebrospinal meningitis and one case of pneumonia with herpes. In all three cases definite lesions were found in the sensory ganglia supplying the herpetic areas.

In addition, I have seen in the wards of the Lakeside Hospital, in the service of my colleague, Dr. John H. Lowman, two unusual examples of facial herpes complicating non-fatal pneumonia.

Report of Cases: Herpes Complicating Pneumonia.

Case I. *Summary: Herpes of the skin of the right side of the nose, especially marked near the inner canthus of the right eye, occurring in a child with pneumonia complicating typhoid fever; degenerative and exudative changes in that portion of the right Gasserian ganglion, giving rise to the nerves supplying the skin of the upper portion of the nose; left Gasserian ganglion normal.*— T. W., male, aged four years, was admitted on March 26, 1903, to the Lakeside Hospital, service of Dr. John H. Lowman, after an illness of thirteen days. He was drowsy and apathetic and breathed rapidly. Physical examination showed signs of consolidation of the upper lobe of the right lung. The spleen was enlarged. Widal reaction positive. There was a well-marked crop of herpes near the inner canthus of the right eye. On the morning of March 31st

[1] Read by title at the Twentieth Annual Meeting of the Association of American Physicians, Washington, D. C., May 17, 1905.

sloughing of the right cornea was recorded. Death occurred at 11.45 P.M., March 31, 1903.

Clinical Diagnosis. Typhoid fever, acute croupous pneumonia of the right lung, herpes of the right side of the nose, sloughing of the right cornea.

Anatomical Diagnosis. Typhoid fever (ileotyphus), hyperplasia of the mesenteric lymph nodes and the spleen, acute croupous pneumonia of the right lung (all three lobes), acute serofibrinous pleurisy, emphysema of the left lung, focal necrosis of the liver, cloudy swelling of the heart, liver, and kidneys. Herpes of the right side of the nose, sloughing of the right cornea, congestion, hemorrhage and acute degenerative and interstitial inflammation of the right Gasserian ganglion.

Bacillus typhosus was isolated from the spleen and gall-bladder, and staphylococcus pyogenes aureus from the lungs, heart blood, and liver.

The autopsy was begun ten hours after death. The detailed description of the autopsy findings will be omitted. The Gasserian ganglia were of ordinary size. The veins about both were congested. The capsules and nerves of both were free from signs of inflammatory exudation. There was no meningitis.

Histological Examination of the Gasserian Ganglion and the Fifth Nerve. Right Gasserian Ganglion: There was marked congestion of the veins along the convex border of the ganglion. Here, corresponding to a portion of the origin of the superior maxillary muscle of the fifth nerve, there was an area showing marked degeneration of the ganglion cells and infiltration of the interstitial tissue with leukocytes. The fifth nerve and its branches showed no degenerative or inflammatory changes. The *left Gasserian ganglion* and fifth nerve were normal.

CASE II. *Summary: Herpes of the right upper and lower lips, the right upper and lower eyelids, and the right side of the neck*—i. e., *of the regions supplied by the right Gasserian and the right third cervical ganglia, occurring during an attack of acute croupous pneumonia, ending in recovery.*—Mrs. H. C., aged fifty-eight years, was admitted to the Lakeside Hospital, service of Dr. J. H. Lowman, on May 7, 1904, with the physical signs of acute croupous pneumonia of the lower lobe of the right lung, which later involved the entire lung. She was taken ill on May 3d, with a chill and pain in the right side of the chest. On admission there was an extensive crop of herpes involving both the upper and lower lips (most marked on the right side) and the right upper and lower lids of the right eye. There was conjunctivitis with granular lids on this side.

On the sixth day of her illness a crop of herpes appeared on the right side of the neck two inches below the angle of the jaw.

The patient recovered, so there was no opportunity to examine the sensory ganglia. The herpes ran the usual course of the so-called

herpes zoster. In the light of our previous cases and of those of meningitis reported below, it is evident that the patient had extensive lesions of the right Gasserian and of the right third cervical posterior root ganglia.

CASE III. *Summary: Herpes of the left lower eyelid occurring in the course of acute croupous pneumonia.*—In this man, also in the service of Dr. J. H. Lowman, there was herpes orbicularis occurring in a typical attack of acute croupous pneumonia, ending in recovery.

Herpes Complicating Cerebrospinal Meningitis.

CASE IV. *Summary: Epidemic cerebrospinal meningitis, with herpes of the right side of the face and neck, and of the left upper lip, and the vestibule of the nose and of the head and soft palate, regions supplied by both Gasserian and the third right cervical posterior root ganglia.*—D. L., male, aged twenty years, entered the Lakeside Hospital, service of Dr. H. H. Powell, October 27, 1904, complaining of severe pain in the head and the right side of the body. He had always been well until October 20th, when he was taken ill with chilly sensations and pain in the head and body.

Four days later he suffered severe burning pain in the right side of the neck. Later at this point a rash developed, followed by a large crop of herpetic vesicles. On admission there was marked rigidity of the neck, hyperæsthesia, and marked herpes, involving a large area on the right side of the neck below the angle of the jaw. Herpes later developed on the right cheek, near the ear. Kernig's sign was present. The diplococcus intracellularis meningitidis was isolated from fluid removed at lumbar puncture. Death occurred November 11, 1904.

Clinical Diagnosis. Epidemic cerebrospinal meningitis with facial and cervical herpes.

Autopsy. The autopsy was begun one hour after death.

The following is abstracted from the autopsy protocol: The body is that of a white male, 167 cm. long. There are extensive herpetic eruptions involving the right cheek just in front of the ear, the right side of the neck, the left upper lip and vestibule of the left nostril and the mucous membrane of the hard and soft palate on both sides. The eruption of the lip and nose is in the vesicular stage. That on the face and neck is covered with dry crusts. In the mouth the eruption is macular and pustular.

Nervous System. The dura and pia arachnoid are congested. Over the surfaces of the medulla and pons there is a thick fibrinopurulent exudate of gelatinous consistency. At the base of the brain and in the lateral ventricles there is a considerable amount of turbid fluid. The nerves at the base of the brain are enveloped in the exudate.

Gasserian Ganglia. Both are surrounded by a thick purulent exudate. The bloodvessels are congested.

Spinal Cord. The membranes of the cord are bathed in a turbid fluid. The pia arachnoid is covered with a fibrinopurulent exudate, which extends to many of the nerve roots. The cord on section shows no appreciable changes. The third right cervical ganglion is larger than its fellows of the opposite side.

The other organs show no changes of present interest and their description is, therefore, omitted. The diplococcus intracellularis meningitidis was isolated in pure culture from the cerebrospinal exudate.

Microscopic Examination of Nervous System. The central part of the convex border of the ganglion—*i. e.*, that portion corresponding to the origin of the superior maxillary branch and possibly a portion of the inferior maxillary branch is the seat of extensive degeneration and destruction of ganglion cells, with leukocytic infiltration.

The affected ganglion cells are cloudy, stain poorly and are often hyaline. Some cells are swollen and others are shrunken. In those less affected the nuclei show no changes. In markedly degenerated cells the nuclei may be eccentric and some stain diffusely. The leukocytic infiltration is most marked in the interstitial tissue, but some ganglion cell spaces contain leukocytes. The plexus of nerve fibres coming from this portion of the ganglion are surrounded with a fibrinopurulent exudate. Sections of the sensory root of the fifth nerve show no recognizable changes, when stained in either methylene blue and eosin or by Weigert's myelin sheath method.

Left Gasserian Ganglion and Fifth Nerve. In this ganglion similar changes are present and in the same portion of the ganglion as described in the right. The sensory root of the fifth nerve shows small scattered areas of cellular infiltration.

The Third Right and Left Cervical Ganglion and Posterior Root Nerves. The right ganglion is the seat of numerous small areas of ganglion cell degeneration and of interstitial and periganglion cell cellular infiltration. The changes are best marked at the distal end and at one side of the ganglion. The right posterior root is surrounded and infiltrated by large numbers of leukocytes. The left posterior root is similarly but less intensely affected. The left ganglion is normal.

Sections of the cord made at various levels show marked meningitis. The other ganglia are free from changes.

Anatomical Diagnosis. Acute epidemic cerebrospinal meningitis, due to diplococcus intracellularis meningitidis. Degenerative and exudative changes in both Gasserian and in the third right Gasserian ganglia, herpes of the hard and soft palate, the left upper lip, the vestibule of the nose, the right cheek and the right side of the neck.

In regard to the lesions in the third right cervical ganglion, it is clear that the infection made its way along the posterior nerve roots. In the case of the Gasserian ganglia the route of the infection is not

so clear, but it is evident that the inflammatory process is more marked in the nerve bundles about the ganglion than in the latter structure itself. It is to be noted that the distribution of the herpetic lesions corresponds exactly with the ganglionic lesions.

CASE V. *Summary: Trifacial neuralgia of the right side, suppuration of the sphenoidal sinuses; brain abscess and acute cerebrospinal meningitis, due to an actinomyces; herpes of the posterior and lateral cervical regions of the side.*—E. W., coachman, aged forty-six years, was admitted on February 11, 1905, to the Lakeside Hospital, service of Dr. J. H. Lowman, complaining of severe trifacial neuralgia of the right side. He denied having had any previous illness, except whooping-cough in childhood. He stated that he had been in good health until two weeks before admission, when his illness began with severe headache and backache. There was a slight chill, but no cough or other symptoms of disease of the respiratory tract. Ten days before admission he developed some pain, paroxysmal in character, and tenderness on pressure of the right side of the face and head. Remedies applied in the hospital relieved this pain.

On February 13th, two days after admission, he developed symptoms pointing to brain abscess on the right side and to cerebrospinal meningitis. At lumbar puncture 70 c.c. of turbid fluid were obtained. From the fluid Dr. Louis W. Ladd isolated an actinomyces, which will be described in a future paper.

At this time there appeared well-marked herpes of the skin over the capital portion of the trapezius muscle and the angle of the scapula on the left side. There was no herpes elsewhere. Death occurred February 17, 1905.

Clinical Diagnosis. Abscess of the right side of the brain, cerebrospinal meningitis due to an actinomyces. Herpes of the neck.

Autopsy. The autopsy was begun a few hours after death. As this case will be reported in full in another paper, the present descriptions of the pathological findings will be restricted to the lesions of the right fifth nerve and Gasserian ganglion and the third and fourth cervical ganglia and their roots.

Abstract of the Autopsy Protocol. The right Gasserian ganglion is of ordinary size. The sensory nerve of the fifth nerve is swollen and is marked by dark-red streaks. The veins about the ganglia were markedly dilated.

Histological Examination. Some of the veins of the capsule of the ganglion are found to be congested, but there is no hemorrhage. The ganglion cells stain normally, are not shrunken or invaded by cells. There is no infiltration of the interstitial tissue. In sections of the root of the fifth nerve stained with eosin and methylene blue, marked inflammatory lesions are found. The small veins and capillaries are congested and widely dilated. There are numerous areas of hemorrhage, which distort the nerve tissue. In many

sections there are large accumulations of red blood corpuscles, leukocytes, and large oval cells about the dilated bloodvessels. The large cells, which are most numerous are evidently proliferated connective-tissue cells. In sections stained by Weigert's myelin sheath method, there is marked breaking up and even disappearance of myelin sheaths about many of the fibres about the areas of hemorrhage and inflammation. The left Gasserian ganglion and fifth nerve show no pathological changes.

Third Cervical Ganglia and Posterior Roots. The left ganglion is larger than its fellow of the opposite side. Histologically, the changes are marked. They consist in degenerated and necrotic changes in ganglion cells and in proliferative and exudative changes in the interstitial tissue. The changes are confined largely to the proximal end and to one side of the ganglion. In the affected areas the capillaries and small veins are dilated, and here and there small areas of hemorrhage are seen. The degenerative changes of the ganglion cells vary from swelling and cloudiness, with failure of the granules to stain, to hyaline change and complete necrosis. Some cells show larger and smaller vacuoles. The necrotic cells are shrunken, and their nuclei do not stain. The nuclei of some of the degenerated cells stain diffusely. There is proliferation of the cells of the spaces about the ganglion cells. The latter are not, however, invaded by cells. The right ganglion is normal.

Posterior Nerve Root. Left. The inflammatory changes here are extreme. The nerve is surrounded by a thick fibrinopurulent exudate, and in many places there are larger and smaller areas of purulent exudation in the nerve itself. This is associated with both hemorrhages and proliferation of nerve cells. Similar but less intense changes are found in the right posterior root.

The Fourth Cervical Ganglia and Nerve Root. The left ganglia and its root show the same marked degenerated and inflammatory changes described in the third left. The right ganglia is normal, but its root shows marked perineuritis and endoneuritis. The other ganglia are normal.

Spinal Cord and Meninges. Sections of the cord and meninges cut at various levels show meningeal inflammation in varying degree. They are most marked at the level of the third and fourth cervical ganglia. Here the pia arachnoid is the seat of a marked fibrinopurulent exudation, which extends along the nerve roots on both sides. The polymorphonuclear neutrophilic leukocyte is the most common cell in the exudate, but large and small mononuclear leukocytes are also present. There are also numbers of large cells with single oval nuclei. A few long, thread-like organisms are found.

The cord shows no inflammatory changes, and its ganglion cells appear normal.

Anatomical Diagnosis. Actinomycotic abscess of the right occipital lobe rupturing into the right lateral ventricle. Suppurative

inflammation of the sphenoidal sinuses, acute seropurulent cerebrospinal meningitis. Acute neuritis of the fifth nerve and of the third and fourth and other posterior nerve roots. Acute inflammation of the third and fourth posterior root ganglia of the left side; herpes of the left side of the back of the neck and of the left scapular region. Slight actinomycotic bronchopneumonia.

SUMMARY. A review of these cases shows a complete correspondence between the situation of the herpetic lesions and the ganglionic changes. In each case the distribution of the herpes was limited to areas of skin or mucous membrane supplied by the ganglia, which were the seat of the degenerative inflammatory lesions. In those cases with herpes of areas supplied by nerves from the Gasserian ganglion this relation is even more precise. In Case I., for instance, with herpes on the nose near the inner canthus of the eye, the ganglionic lesion was limited to the point of origin of the superior maxillary nerve. In Case IV., with multiple herpetic lesions of the head (nose, upper lip, cheek, hard and soft palate), the lesions of the Gasserian ganglia again corresponded completely to the portion giving origin to the nerves supplying these parts. In Cases II. and III., though unsupported by anatomical examination, in view of the findings in the other cases, the inference that the herpes was associated with lesions of the Gasserian ganglia seems justified.

Case V. is of particular interest, for it demonstrates that, just as in spinal meningitis with involvement of the nerve roots, herpes does not occur unless the inflammatory changes extend to the ganglia; so in marked neuritis of the sensory root of the right fifth nerve, without appreciable changes in the Gasserian ganglion, herpes of the part supplied by this ganglion does not occur. In this case, under these conditions, there was severe trifacial neuralgia without herpes. Degenerative changes, with or without inflammatory lesions of the sensory ganglia, are therefore necessary for the excitation of the nervous impulses upon which the production of the herpetic lesions depend.

Cases IV. and V. also confirm the opinion expressed in my previous paper that the herpes of cerebrospinal meningitis is due to inflammatory lesions of the sensory ganglia.

The cases reported in this article furnish additional proof to support the position that the ordinary herpes zoster, as well as the herpes of pneumonia and cerebrospinal meningitis, is a pathological condition dependent upon definite lesions of certain sensory ganglia, which may be caused by a variety of agents acting in different ways. The herpes is dependent upon the ganglionic lesions, and apparently does not vary with causes of the latter, whether they are due to embolism, thrombosis, hemorrhage, invasion by tumors, microorganisms and other toxins or to other poisons. The ganglionic changes in the cases of herpes complicating pneumonia and cerebro-

spinal meningitis studied by me are identical with those described by Head and Campbell in their acute cases of so-called spontaneous herpes zoster. In the herpes of meningitis the ganglion changes are probably commonly due, as pointed out by Councilman, Mallory, and Wright, to an extension of the inflammatory process along the nerve roots to the ganglia. In pneumonia the matrices morbi are apparently brought to the ganglia by the circulation.

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A CASE OF SYRINGOMYELIA WITH DOUBLE OPTIC NEURITIS.

BY T. H. WEISENBURG, M.D.,

AND

JAMES THORINGTON, M.D.,

OF PHILADELPHIA.

OPTIC neuritis as a complication of syringomyelia is of such unusual occurrence that a report of such a condition even without necropsy should be of interest.

We have been able to find only two similar cases in the literature, one by Bullard and Thomas, reported in this JOURNAL in 1899, and the other by Saxer.[1] Although neither of these instances were diagnosed during life, their clinical histories to a large extent resembles ours. A brief *résumé* of these cases is of interest.

Boy, aged six and one-half years. His family and the past history of the patient were unimportant. At three years of age severe headache and a little later vomiting appeared. These symptoms gradually increased in severity and a year after they began marked double optic neuritis developed, this being followed by optic atrophy. Ten months after the blindness began, a sudden paralysis of the lower limbs appeared, followed by anæsthesia and flexor contractures in the lower limbs and disturbances in the function of the bladder and rectum. The headache, blindness, and the vomiting persisted

[1] Beiträg. z. path. Anat. u. z. allgem. Path., Bd. XX. No. 2.

until death, which was three years after the beginning of the symptoms. The pupils were dilated and did not respond to light or accommodation. There was a paralysis of both external recti. Convergence was normal. A temporary paralysis of the left seventh nerve had been present. Hearing and taste were not affected, and bulbar symptoms were not present.

At the necropsy a cavity was found in the spinal cord extending from the third lumbar segment to the pyramidal decussation. The lateral, third, and fourth ventricles were markedly dilated.

In Saxer's case a girl of sixteen had severe pain and considerable weakness in the lower limbs. There was marked double choked disk with converging strabismus and disturbance of movement, especially in a lateral direction of the left eye. At the necropsy a syringomyelic cavity was found extending to the upper part of the cervical cord, and in the brain a marked congenital internal hydrocephalus was present.

The history of our case is as follows: A girl, aged sixteen years, has been under our observation for the past six months. Her paternal grandmother died of cancer and her paternal grandfather of "paralysis of the brain." Her mother died of hemorrhage one week after the birth of the patient. Has two brothers and one sister living and well. One brother died of fever at the age of seven.

The patient was born at full term in easy labor and was said to be a sickly babe. Had many of the ordinary diseases of childhood, but was comparatively well until the age of seven, when she started to grow exceedingly fast, being now about six feet tall. She would, however, play and behave much like other children until she was twelve years of age.

Mentally she had always been considered peculiar, and was said to have epilepsy when a child. Since the age of twelve she has gradually become stupid and her powers of attention, imitation, and memory have become very poor. She is very indolent, obstinate in some things; is very careless of her clothing, and spends most of her time sitting and staring. Speech is normal, there being entire absence of bulbar phenomena.

Coincident with the appearance of the mental symptoms a decided unsteadiness appeared in her walking, and when first examined several months ago she was barely able to walk with assistance, dragging both legs, especially the left. At present she is chair-fast.

She has been complaining of more or less frontal headache for the past two years, and occasionally vomits forcibly. Has not had nausea, dizziness or convulsions, and when first made to stand did not stagger. The eye symptoms have come on during the past two years until now she is completely blind in her right eye and almost so in the left.

The patient while sitting always inclines her head forward and to the left. There is a lateral spinal curvature to the right in the

dorsal region. She is extremely thin but not emaciated, and there is no particular atrophy anywhere. The skin is dry and scaly.

Movement is possible in all directions in the upper limbs, but they are weak. The grasp of each hand is poor. The bicep reflexes are present in each side but are much diminished, while the triceps and wrist reflexes are absent. There is ataxia of both upper limbs, more marked in the left. The lower limbs are contractured in flexion at the knees. Is able to move her ankles weakly. The patellar and Achilles jerks of each side are much and equally exaggerated, and ankle clonus is occasionally present. The Babinski reflex was not obtained, the toes not moving in plantar irritation.

FIG. 1

Photograph of the patient, illustrating the constant deviation of the head to the left.

Sensation for all forms is normal over the face. In irregular areas in the left forearm, arm, shoulder, and chest, both in front and back, touch is properly recognized, but pinprick and both heat and cold are not recognized, or are called touch. Sensation seems normal over the rest of the body.

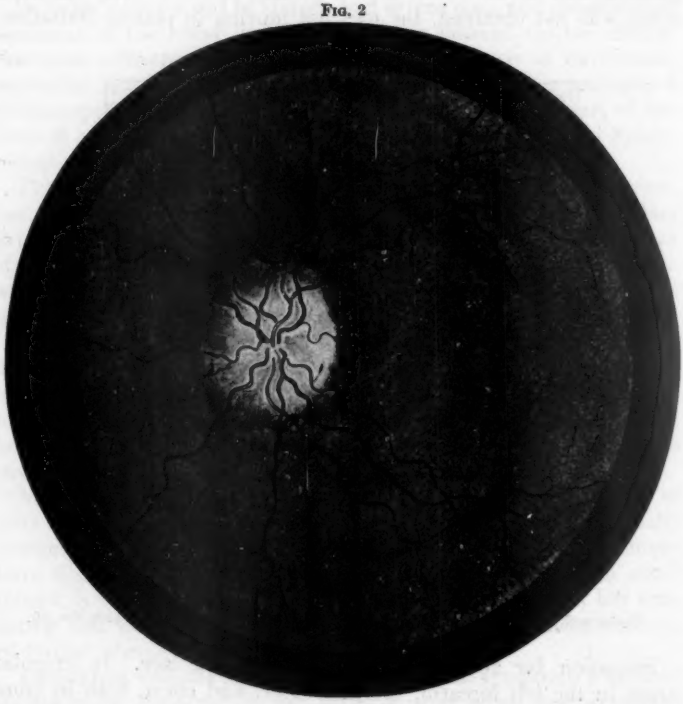
There is incontinence of urine and feces at times, but it is a question whether this is not due to her mental condition.

The tongue is protruded straight, there being no tremor or atrophy. The facial nerves are normal, and the masseters contract well in either side. Hearing seems disturbed on the left side.

The following is Dr. Thorington's report from examinations made March 28, May 2 and 17, 1905: Both eyes under the influ-

ence of atropin. Pupils are dilated equally round, 8 mm. in diameter. Eyeballs are not prominent. There is no ptosis or nystagmus. The vertical width of palpebral fissure in the centre is 8 mm. When either eye is brought to the median line the upper lid covers the upper portion of the cornea to the extent of about 2 mm., and at the same time the sclera is exposed for about 1 mm. in width between the lower edge of the cornea and the upper edge of the lower lid. In a state of repose each eye is decidedly divergent; the temporal edge of each cornea being hidden for 1 or 2 mm. in the outer can-

FIG. 2

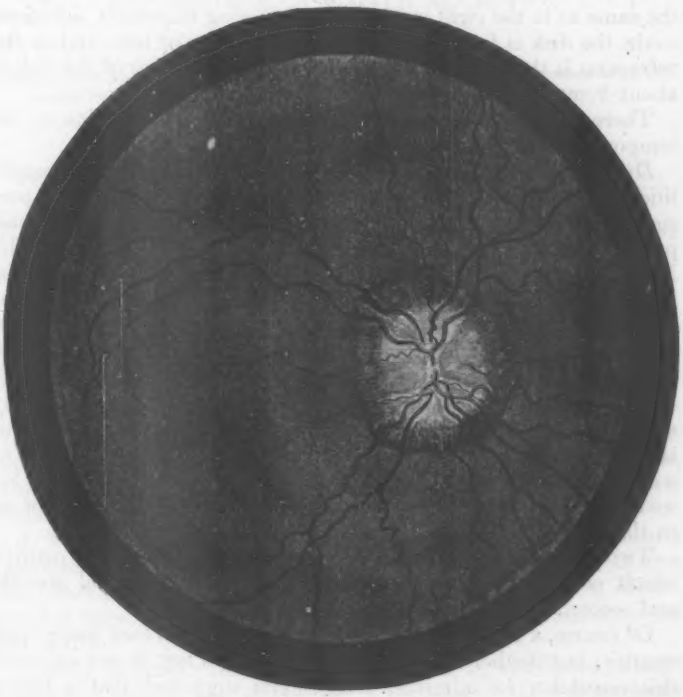


thus. Neither eye will converge or change its position from divergence when the finger is advanced toward the nose in the median line. The tension of each eye is normal, and there are no other gross external changes present. When not under the influence of atropine the pupils are 5 mm. round and the irides respond slightly to light and accommodation, the left a trifle more than the right. There is weakness of both external recti. Associated movement upward and downward is of normal extent, but are weak because she is unable to fix the eyeballs in these directions for any length of time.

Apparently the right eye is blind. The patient states that she cannot see the small five-volt electric light when held close to the eye. Neither does the eye wink unnaturally when the finger is moved slowly or rapidly close to the eye.

The left eye is not blind and the patient is able to count fingers eccentrically at a distance of ten inches. The field of vision is apparently limited to the nasal field, though this is not positive, as the patient's mental condition is too uncertain for definite answers.

FIG. 3



Ophthalmoscopic Examination of the Right Eye. The cornea, lens, and vitreous are clear, no opacities present. Eye-ground "flannel red" in color. There are no hemorrhages present nor are there any indications that there ever had been any hemorrhages. The macula is without any changes and the perimacular region is normal. The disk is quite prominent, round, and its edges striated, hazy, and of a dirty gray color. The central portion of the disk is chalky white in color. The apparent width of the disk as it extends into the surrounding eye-ground is about twice that of the normal

disk. The retinal vessels are much smaller than normal, the veins are not unusually tortuous at the present time and the light streak in the veins and arteries is seen only upon the disk and extending out a very short distance from it. The elevation of the disk is best seen with a plus four diopter lens at the sight hole of the ophthalmoscope and the surrounding eye-ground is seen with a plus two; this gives a swelling of the disk of about two diopters, which would represent about $\frac{2}{3}$ of a mm. The refraction of the eye is therefore two diopters of hypermetropia without any astigmatism.

Ophthalmoscopic Examination of the Left Eye. The findings are the same as in the right eye with the following important additions —viz. the disk is best seen with a plus five diopter lens, and as the refraction is the same as in the other eye, the swelling of the disk is about 1 mm.

There is considerable broken pigmentation in the retina to the temporal side of the disk.

Diagnosis. Well-developed papillitis with beginning postpapillitic atrophy, much more advanced in the right eye, which was presumably the eye primarily involved. The papillitis, which is still present in each eye and well illustrated in the colored sketches by Miss Washington, is apparently an unusual variety of papillitis, and is known as "engorgement" papillitis of von Gräfe in contradistinction to the more common variety of papillitis known as inflammatory. This diagnosis is substantiated by the (*a*) absence of hemorrhages, (*b*) the absence of macular changes (macular figure), (*c*) by the characteristic swelling of the disk which ceases abruptly at the edge. Of course, this diagnosis of "engorgement" papillitis is not always positive, for the two varieties of papillitis are not as widely separated ophthalmoscopically as we might wish, and yet with the diagnosis of syringomyelia there is little if any doubt as to the correctness of this opinion.

Two possible causes can be mentioned to explain the optic neuritis which complicates syringomyelia. First, an intracranial growth, and second, an internal hydrocephalus.

Of course, a tumor almost anywhere in the brain may cause optic neuritis, but neither in the two reported cases nor in our case can this possibility be admitted. Hoffmann suggested that a tumor situated in the medulla oblongata, and which formed the starting point of a syringomyelia, could easily cause optic neuritis. This of course may be so, but in the cases reported by Saxer and Bullard and Thomas the syringomyelic cavity did not extend beyond the lower part of the pyramidal decussation.

More probably as in the cases of Saxer and Bullard and Thomas, internal hydrocephalus caused the optic neuritis in our case. Schlesinger in his admirable monograph on syringomyelia expresses himself of the opinion that hydrocephalus is a frequent complication of syringomyelia, and mentions eleven such cases. He further states

that through pressure caused by the increased amount of cerebrospinal fluid there may be palsy of different cranial nerves. This is undoubtedly the explanation for the paralysis of the external recti muscles and the possible weakness of associated movements present in our case.

CHRONIC ANTERIOR POLIOMYELITIS, WITH THE REPORT OF A CASE WITH NECROPSY.

By George A. Moleen, M.D.,

ASSISTANT IN NEUROLOGY, DENVER AND GROSS COLLEGE OF MEDICINE; NEUROLOGIST TO MERCY HOSPITAL AND DENVER CITY AND COUNTY HOSPITAL, DENVER, COLORADO,

AND

William G. Spiller, M.D.,

PROFESSOR OF NEUROPATHOLOGY AND ASSOCIATE PROFESSOR OF NEUROLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

(From the Denver and Gross College of Medicine and from the Neuropathological Laboratory of the University of Pennsylvania.)

CLINICAL NOTES AND REMARKS BY DR. MOLEEN.

Owing to the diversity of opinion with reference to the classification of spinal-cord lesions attended with muscular wasting, with or without spasticity, and with or without the presence of the deep or tendon reflexes, the assigning of the following case presents a somewhat difficult problem, and for this reason it is deemed wise to first detail the clinical notes of the case before discussing those points, which, to the author, were obstacles in arriving at an appropriate clinical diagnosis.

J. Ten W., aged thirty-seven years, laborer, though he did mostly upholstering work, was first seen October 3, 1903, at which time the following notes were made: He was born in St. Clair, Minn., but has been in Colorado six or seven years, and did not come for his health.

Family History. He denies all diseases of childhood, except measles, which he had at the age of ten years. He was perfectly well until 1890, when he had an attack of la grippe, and he had another in Colorado three years ago. His calloused hands bear him out in the statement that he has done hard work, and he says that he has been exposed in the mountains to rough weather until a few years ago, though he denies rheumatism or pneumonia. He admits having contracted gonorrhœa, but firmly denies syphilitic infection. It may be stated, however, that a physician related to him informs me that he treated him for syphilis twenty years ago.

Present History. About two weeks ago, without chill, pain, cold, fever, numbness, or the slightest symptom of an acute character,

he noticed upon arising in the morning that his left foot felt heavy and that he was "limping."

He insists that he was perfectly well at the time and that the weakness was his only cause for complaint. He is certain that he is no worse to-day than when he first noticed his trouble. He has no difficulty in passing his urine nor in emptying his bowel.

FIG. 1

Showing the wasting of the lower limbs and foot-drop.

Examination, October 6, 1903, gave the following results:

He is a short—five feet, three inches—well-developed man, though he shows his age and hard work. His weight is 120 pounds.

In walking the left foot is raised considerably higher than the right, and with a jerky exaggerated flexion of the knee the foot is planted squarely on the floor with a tendency to strike the toe first.

Standing with the eyes open and the feet together, there is no perceptible swaying, which is but slight when the eyes are closed.

In the sitting posture, with lower limbs hanging, the "foot-drop" is noticeable on the left side.

There is no ataxia in the arm nor trunk muscles.

The calf of the left leg is somewhat atrophied and the muscles flaccid, though especially noticeable is the wasting of the muscles supplied by the peroneal nerve. The dorsum of the left foot, from the prominence of its tendons, seems more wasted than the right.

The circumference of the largest part of the calf: right, 12¾ inches; left, 11½ inches. Of the thigh: right, 17½ inches; left, 15¾ inches.

Electrical reactions: Galvanic battery is out of order and reactions cannot be taken. Faradic irritability is greatly diminished in the lower part of the left leg, otherwise it is normal throughout this limb. With the slowly interrupted current no contraction of the muscles supplied by the peroneal nerve can be obtained, even with the strongest current.

Reflexes: Knee-jerks, right is increased, especially on reinforcement. Left is slightly more increased than the right, but the knee-jerks were not increased to the degree commonly observed in spastic paralysis. Ankle clonus is absent. Tendo Achillis reflex: Right is present and about normal. Left is absent.

Deep reflexes of the forearm, flexors and extensors: Right are present. Left also and slightly increased. Biceps, triceps, and deltoid, same. Dynamometer (Tiemann, inner scale): Right = 280; left = 280. The man is right-handed. Masseter reflex is absent.

Superficial reflexes: Plantar: right is present; left is very slight. There is no evidence of the Babinski phenomenon. Cremasteric reflex: Right is present; left also is present, though not so marked as right. Lower abdominal reflex: Right is slight; left is very slight. Epigastric reflex is present.

Sensory phenomena are normal throughout the body (tactile pain, pressure, temperature, and postural senses taken).

Special senses: Eyes, all external ocular motion is normal and without nystagmus. Pupils are equal and respond actively to light and accommodation. Fields of vision are apparently normal. Fundi: There are no retinal changes, and the disk is well outlined in either eye. Hearing (watch): Right = 6–24; left = 8–24. The tuning-fork is heard best in the closed ear, and aerial conduction is greater than that of bone. Taste and smell are seemingly not impaired. The tongue is protruded in the median line, without tremor, and there is no difficulty in speech.

A diagnosis of anterior poliomyelitis was made at this time and he was under observation until January, 1904. During this time there was no apparent change in his condition, and it may be said that, though repeatedly examined, there was no wasting to be noticed in the hand nor in any other part of the body, nor was

fibrillation to be seen at any time, these symptoms having been expected because of the absence of improvement.

He was not seen again until January 21, 1905, when the following notes were taken:

The face is apparently drawn, probably due to emaciation, and moderate emotion (laughter) is not evidenced in the facial expression. All voluntary motion of the facial muscles, though weak, is equal on the two sides. The tongue is protruded about half an inch beyond the incisor teeth, shows a decided fibrillary tremor throughout, and is markedly furrowed from wasting. It is protruded in the median line.

He responds correctly to questions asked him, though with very slow enunciation, drolling all words requiring the use of the pharyngeal and labial muscles, but more particularly the lingual.

He states that six weeks ago he "had his palate cut" (referring to the uvula), from which time he noticed difficulty in swallowing and speaking.

FIG. 2

Showing the wasting of the hands and forearms.

There is to be noticed in the most prominent muscles—*e. g.*, biceps, deltoid, pectoral, gluteal, etc., linear depressions parallel to the muscle fibres, apparently wasted strands, between which lines of twitching are to be seen. This twitching is also to be plainly seen in the spinal muscles. Tapping the muscles increased the frequency though not the degree of the twitching.

The greatest wasting is to be observed in the hand muscles on both sides, more particularly the adductors of the thumb. The thenar and hypothenar eminences are completely wasted, and on extending the hands a decided, somewhat coarse tremor of the right thumb is noticeable (Fig. 2).

The left lower extremity is smaller in size than the right, and the group of muscles innervated by the left peroneal nerve is entirely wanting.

Plantar flexion of the left foot is somewhat weaker than of the right, while no dorsoflexion of the left foot can be accomplished.

The muscular strength in the shoulder, arms, and forearms is fairly well preserved and equal. Dynamometer, right = 110; left, = 100.

The man walks raising the left knee markedly higher than the right, and the left foot is swung farther forward and placed flatly on the floor and turned slightly outward. His gait is little if at all altered upon closing the eyes. He is able to stand with the feet together and eyes open, though he sways slightly, and the swaying is somewhat increased when the eyes are closed. The increased effort in the latter instance seemingly excites a fine tremor of the face and neck muscles.

The arm and trunk muscles are free from ataxia.

Measurements of the extremities: Arms, 4 inches above the olecranon; right = 8¾ inches; left = 8¼ inches. Arms, 4 inches below the olecranon; right = 8 inches; left = 7½ inches. Legs, 4 inches below tibial tuberosity; right = 10¾ inches; left = 9½ inches. Thighs, 8 inches below anterior superior spine, right = 15 inches; left = 12½ inches.

Electrical reactions: galvanic (chloride of silver fifty-cell battery was used, sponges moistened in alkaline tepid water, and interruptions made with the handle; current strength in milliampères):

Tibialis anticus: right, KaClC 10, KaOC 10, AnClC none, AnOC none; left, no response to the strongest current; peronei same.

Tibialis posticus: right, KaClC 6, KaOC 12, AnClC 10, AnOC none; left, KaClC 2, KaOC 3, AnClC 5, AnOC 20.

Flexor carpi radialis: right, KaClC 2, KaOC 15, AnClC 6, AnOC 25; left, KaClC 2, KaOC 20, AnClC 3, AnOC 15.

Extensor communis digitorum: right, KaClC 4, AnClC 3; left, KaClC 4, AnClC 2 (weaken rapidly).

Both the right and left deltoid muscles give anodal and cathodal contractions at 3 milliampères.

Masseters are equal: KaClC 1½, AnClC 3½. Sternocleidomastoid muscles are equal: KaClC 2, AnClC 3.

There can be no responses obtained from the thumb muscles of either hand with the strongest currents.

Faradic: (No. 8 chloride of silver battery, No. 2 secondary coil, 26 wire; two cells in circuit and current strength indicated in fractions of the rheostat circumference, unless otherwise indicated).

Tibialis anticus: Negative, right, ⅓; left, none with full current. Positive, right, ½; left, none with full current.

Rapid interruptions the same.

Tibialis posticus: Right, ½; left, ½ (negative).

Extensors of both legs respond equally to ½; flexors, ¾.

Flexor communis digitorum: left, ⅓; right, same.

The muscles of both arms and forearms show an increased irritability. Facial muscles are about normal, electrically.

Reflexes: Knee-jerks, right, increased; left, also. The effect is little changed by reinforcement. A slight ankle clonus of short duration is present in the right foot, which is very easily exhausted. Left absent. Deep reflexes of the forearm: Flexors and extensors present, those of the left side are seemingly more pronounced than those of the right side. Biceps, triceps, deltoid, and pectoral reflexes are present. Masseter reflex is absent.

Superficial reflexes: Plantar, right is present; left is absent. There is no evidence of the Babinski phenomenon, and the dorsal foot reflex lately described by Mendel[1] is negative. Cremasteric reflex: right is slight; left is absent. Lower abdominal reflex apparently is absent. Epigastric reflex is slight.

All sensory phenomena (tactile, temperature, pain, pressure, and postural) are normal and equal.

Owing to lack of control of the tongue, it is difficult to accurately test the sense of taste, though it is seemingly normal, as is also the sense of smell.

Eyes: Pupils are equal and respond equally to light and accommodation. Ocular motion is equal in all directions. The fields of vision (taken with the hand) are evidently not contracted. The disks, while pale, show no degeneration and the vessels are not changed.

Hearing is about as previously recorded.

The foregoing notes were taken during several examinations made between January 21 and 29, 1905, to which the following general observations may be added: Inability to control emotion; the extremes only were evident in the facial expression; slight laughter was often followed by tears without provocation; increasing dysphagia and dysarthria; increasing difficulty in coughing and expectorating apparently due to lack of control of the respiratory, pharyngeal, and lingual muscles.

When seen January 29, 1905, at 1 P.M., the temperature was 99.5° and pulse 100, and he was sleeping quietly. Refusing nourishment, he slept the greater part of the afternoon, death taking place at 7 P.M. of the same day, the increase in pulse and respiration rate and volume being the only change noticed, the attendants are certain, however, that no marked changes in respiration (*e. g.*, laryngeal spasm, Cheyne-Stokes breathing) were to be noticed.

Autopsy was made three hours after death. The examination was limited to the spinal cord and brain. The body was quite warm. The spinal cord and brain were removed, the cerebellum, brain stem and cord being retained for examination. The membranes were not adherent, no vascular change was noticed, and the ventricles were apparently normal. No gross changes were observed in the cerebral hemispheres. The retained portions were submitted to Dr. William G. Spiller for examination.

[1] K. Mendel. Neurologisches Centralblatt, 1904, v. xxiii. No. 5.

SUMMARY. A man, aged thirty-seven years, probably syphilitic, is afflicted with sudden paralysis of the group of muscles innervated by the left peroneal nerve; complete loss of faradic irritability followed in a week, and this was followed by rapid wasting and slight diminution in size of the entire leg; the deep reflexes were present and increased, but not excessively, and in that spinal segment represented by the absolute atrophy they were lost; the symptoms were confined to the left lower extremity and were without change during three months; no fibrillary tremor, sensory disturbance, hand weaknesses, nor cranial nerve symptoms were present. One year later there were slight general emaciation, complete wasting of the thenar and hypothenar eminences, and, to a less extent, of the interossei muscles; atrophy and paresis of the tongue and pharynx, fibrillation throughout the body, including the tongue, and tendon reflexes still moderately increased. There were no marked electrical changes, except in absolutely wasted muscles, and no bladder, bowel, nor sensory disturbances. He was becoming more emotional, dysphagic and without dyspnœa, though he had a rapidly increasing pulse and respiration. Termination was death.

When first observed the recording of the case as acute anterior poliomyelitis, in view of the rapid onset and the absence of evidence of involvement of other portions of the cord, was justifiable. The only points apparently opposed being the age of the patient and the absence of prodromes or febrile disturbance.

The fact that no evidences of extension nor involvement elsewhere could be noticed after three months seemingly supported this diagnosis.

When, however, wasting of the hands, fibrillation, dysarthria, and dysphagia were added after the lapse of a year, one would be justly suspicious of (*a*) progressive spinal muscular atrophy (especially a peroneal type), (*b*) amyotrophic lateral sclerosis, or (*c*) chronic poliomyelitis—three conditions which have been considered by some authorities as synonymous—the extremely wide variations in individual cases notwithstanding.

It seems pretty well established that in pure cases of progressive spinal muscular atrophy the wasting invariably precedes the paralysis, and certainly the great majority of cases first manifest weakness in the hands (nine-tenths, according to Gowers). Conspicuous also is the advent of fibrillary twitching in the gradually weakening muscles, as well as in those about to be attacked, in which the weakness had not been noticed, and in any event before paralysis had supervened.

The electrical reactions in these cases of progressive spinal muscular atrophy persist until the wasting is intense.

Clinically, perhaps, this case more closely conforms to the type known as "peroneal," which since the thesis of Dr. Tooth and the observations of Dr. Hoffmann, has, in the opinion of most author-

ities, merited a separate classification, and some have referred to it as "neuritic" (perhaps more properly "neurotic," from the "Progressive Neurotische Muskelatrophie" of Hoffmann), in view of its occurrence in several members of the same family, in the majority of instances. That it occurs, as a rule, in the second half of childhood—*i. e.*, before the twentieth year of life, seems to be generally accepted, though Oppenheim thinks the commencement may be as late as the fourth decade.

Some observers have used the term "neuritic" advisedly, because of the belief that the peripheral nerves are primarily affected. This is questioned by Dana, who believes the cord to be first attacked, and quotes Marinesco as having recently confirmed this view, mentioning a citation by the same author of a case beginning as a "typical acute anterior poliomyelitis."

As rather against than for the placing of this case under this heading, the following features deserve mention: The occurrence of the disease earlier in life as a rule; usually hereditary involvement; frequent sensory disturbances (pain, numbness, etc.); usually abolition of the tendon reflexes in the extremity affected; slow development; atrophy usually extreme; lastly, conspicuous by its absence in the cases reported is the mention of bulbar symptoms.

As tersely expressed by Dana, the hereditary or "leg type" of progressive muscular atrophy is characterized by its beginning in the legs, by much sensory disturbance, typical degeneration reactions and hereditary or family history.

Is this a case of amyotrophic lateral sclerosis?

It is well before considering this condition to disregard the question of synonymy, and with Oppenheim, Dana, Beevor, and others, return to the original distinctive classification of Charcot. This disease occurs most frequently after thirty, women being more often affected than men; in true types the hands are first affected, and the spasticity is marked; the first symptom is usually rigidity; clonuses, including a masseter clonus, are frequent; flaccid paralysis never inaugurates the disease, and the onset is nearly always gradual. Oppenheim only records an acute beginning; as a rule, each muscle wastes very gradually.

In the study particularly of the clinical side of the case, however strong our convictions may lead us to the heading of progressive muscular atrophy, the consideration of the distinctive points of the third of the "trio," chronic anterior poliomyelitis cannot be overlooked. This line of distinction, one must admit, in the light of our present knowledge, is as yet fine.

While partial recovery is the rule, though more especially in the acute form of anterior poliomyelitis, yet cases do become subacute or chronic, and extension or probably the independent involvement of other segments, including the bulb, are then not uncommon, and in fact bulbar paralysis very frequently closes the scene in all three

of the conditions mentioned—viz., progressive spinal muscular atrophy, amyotrophic lateral sclerosis, and chronic anterior poliomyelitis.

In chronic anterior poliomyelitis the paralysis precedes the wasting, the palsy is absolute, flaccid, without rigidity, and involves groups of muscles physiologically related, while in the other affections previously considered the muscles concerned are anatomically related. Syphilis is a frequent cause in advanced life of the chronic cases; all electrical irritability is rapidly lost in the group of muscles affected, and neighboring muscles are altered in proportion to the degree of subacute extension, this alteration becoming less marked farthest from the cord representation of the principal group involved. A predilection of the peroneal group in all cases of anterior poliomyelitis is notable.

The mention of fibrillary twitching has been purposely omitted heretofore, for the reason that it is seemingly common to all chronic muscular atrophies, and Gowers, in his broad view of the three diseases as one, states that it is not invariable, nor is it confined to this disease; and Oppenheim has to say: "Progressive muscular atrophy can never be diagnosed from fibrillary tremor, as this symptom may occur in healthy persons after excesses, in emaciated individuals when exposed to cold, and in neurasthenic and hypochondriac patients."

While disposed to rest the diagnosis here, I am constrained to admit that against this disposition is the presence or increased activity of the deep reflexes which in the cases previously reported as such was absent; the explanation offered with reference to the electrical alterations in the segments immediately adjacent to the actual lesion, it is reasonable to suppose, will hold good here, and possibly establish a point of distinction with future observation.

It is therefore evident that while no resting place is absolutely fitted for the reception of this particular case, the wide latitude of which chronic anterior poliomyelitis admits, and the fact that here are found fewer opposing factors than in the other mentioned conditions render its placing here at least permissible.

The emotional symptoms at the close of the case are, as noted by Dana, common evidences of bulbar lesions, either primary or secondary.

PATHOLOGICAL NOTES AND REMARKS BY DR. SPILLER.

The case which Dr. Moleen has studied clinically so carefully is worthy of the attention he has given to it. I know of no case with necropsy like it in American or English literature, and it should, therefore, be of value in the study of the muscular atrophies. This is a subject that is still causing much difficulty in classification. The commencement of the symptoms in Dr. Moleen's patient with

peroneal palsy, resembling the neurotic muscular atrophy, is characteristic of certain lesions of the cells of the anterior horns. Baumann,[1] in a clinical study of 85 cases of acute anterior poliomyelitis, has shown that the muscular supply of the peroneal nerve is especially liable to become paralyzed in this disease.

Dejerine[2] reviews the opinions held regarding motor localization within the spinal cord. According to him, it is not segmental (hand, forearm, arm), as Van Gehuchten and De Buck believed; it is not diffuse (Marinesco), each muscle is not separately represented (Sano), but the localization is of the root type. An examination of the diagram given by Dejerine, p. 780, shows that the peroneal supply is represented in the fourth and fifth lumbar and first sacral segments. We can, therefore, understand why, in Dr. Moleen's patient, the paralysis began in the peroneal group.

My report is as follows:

Only the spinal cord and brain stem of this case were sent to me for examination.

Lumbar Region. The white matter by the Weigert hæmatoxylin stain does not appear to be degenerated. The small vessels of the anterior horns are much congested and are, therefore, very prominent by this stain. Those of the posterior horns are also congested, but not so much so as are the vessels of the anterior horns. Small hemorrhages are numerous in the gray matter, especially in the anterior horns, but are also present in the posterior horns. The posterior roots are well stained. The anterior roots of the lumbar and sacral regions show in places distinct degeneration, but these roots are far better preserved than are the cells of the anterior horns. There is no round-cell infiltration within the spinal cord or pia. The nerve cells of the anterior horns are much diminished in number, but those that still persist appear to be almost normal, and only occasionally one is seen showing chromatolysis, displacement of the nucleus, or much pigmentation. A slight recent degeneration in the crossed pyramidal tracts is seen *only* by the Marchi method.

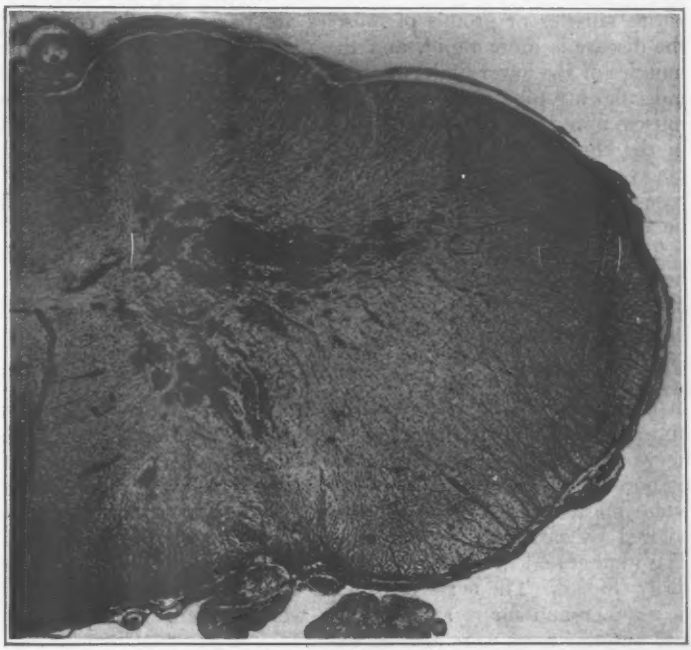
Middle Thoracic Region. Small hemorrhages are numerous in the gray matter, in the posterior as well as in the anterior horns, and are found, but much less numerously, in the white matter near the gray. The Marchi method reveals a very slight degeneration of the crossed pyramidal tracts and a few scattered black dots elsewhere in the anterolateral columns.

First Thoracic and Eighth Cervical Segments. The small hemorrhages are very numerous in the anterior and posterior horns, and are found also in the white matter near the gray. In this portion of the cord the nerve cells of the anterior horns have almost disappeared. There is hemorrhage also within the pia, but nowhere is there any round-cell infiltration.

[1] Monatsschrift f. Psychiatrie und Neurologie, June, 1905, p. 485.
[2] Sémiologie du système nerveux, p. 789.

Medulla Oblongata. Small hemorrhages are numerous here also. Intramedullary fibres of the twelfth nerve have disappeared by degeneration. Unfortunately the nuclei of the twelfth nerves have been injured at the time of the necropsy, but a marked disappearance of nerve cells in these nuclei may be determined. The nucleus ambiguus contains few cells. The intramedullary fibres of the ninth and tenth nerves are much atrophied. A very slight degeneration of the anterior pyramids is seen only by the Marchi method

FIG. 3



Showing the numerous hemorrhages within the gray matter of the spinal cord.

and is less than the degeneration of the crossed pyramidal tracts of the spinal cord.

There are few cells in the nuclei of the seventh nerves and the intramedullary fibres of these nerves are much degenerated. Small hemorrhages are not so numerous in the pons. The cells still persisting in the facial nuclei stain fairly well, except that here and there a cell may be found distinctly degenerated.

A few small hemorrhages are found in the cerebral peduncles,

The important alterations in this case are disappearance of many of the nerve cells of the anterior horns of the spinal cord and motor cranial nerves in the medulla oblongata, of the anterior roots of the lumbar and sacral regions (cervical region was injured), and of the motor nerves of the medulla oblongata, and numerous small hemorrhages in the gray matter, especially in that of the spinal cord.

It is very questionable whether we should make sharp distinctions between chronic anterior poliomyelitis and progressive spinal muscular atrophy. In the first the paralysis is supposed to develop within a few days or a few weeks, the atrophy appears later, and entire muscles or groups of muscles are paralyzed, the course of the disease is more rapid, and the paralysis develops first in the muscles of the lower limbs or shoulders. In the progressive spinal muscular atrophy the paralysis is proportionate to the atrophy, one muscle fibre after another is affected, and the course is longer than in the chronic poliomyelitis. These are distinctions that are not always regarded, and it is very evident that some of the reported cases of so-called chronic anterior poliomyelitis might just as well be labelled as examples of progressive spinal muscular atrophy.

The cases of either type with necropsy are very rare. To Oppenheim the credit of reporting the first typical case of chronic poliomyelitis with necropsy has been justly given. In Oppenheim's[1] first case the weakness began in the right arm. The vessels of the cord were not distinctly altered.

In the case that S. G. Webber[2] reported in 1875 weakness began in the left knee and soon the left leg gave out. Atrophy did not appear until after the weakness. Sensation was not affected. The nerve cells of the cervical region were much diseased and were not numerous. There was some perivascular bulbar infiltration. The white matter of the cord appeared as a homogeneous mass, not colored by carmine; occasionally an axis-cylinder could be seen. The lumbar and thoracic portions of the cord could not be satisfactorily studied. The nerve cells of the hypoglossal nuclei were few in number and many axis-cylinders were swollen. The posterior and anterior roots were also affected.

This case is important, as it was reported about thirty years ago, and clinically seems to have presented the symptoms of chronic anterior poliomyelitis, but pathologically it appears to have been a case of diffuse myelitis. The duration of the symptoms was about one year.

It is true that Nonne[3] included as cases of subacute anterior poliomyelitis those reported by Eisenlohr, and Landouzy and Dejerine, and as a case of chronic anterior poliomyelitis the case

[1] Archiv f. Psychiatrie, 1888, Bd. xix. p. 381.
[2] Transactions of the American Neurological Association, 1875, p. 55.
[3] Deutsche Zeitschrift f. Nervenheilkunde, 1891, Bd. i. p. 186.

of Dreschfeld. These three cases he acknowledges were very different from one another, and he makes three types of chronic anterior poliomyelitis: 1. The circumscribed form (Eisenlohr's case), in which the lesion is confined to a limited area. 2. A form in which paralysis and atrophy *en masse* occur quickly, show a tendency to arrest or to complete restoration, and may possibly be the result of acute or chronic infection (Landouzy and Dejerine's case). 3. A form which progresses slowly and irresistibly with atrophy of nerve cells without secondary atrophy of peripheral nerves (Dreschfeld's case) or with this atrophy (Oppenheim's case).

Oppenheim, in a later paper, does not accept as cases of chronic or subacute anterior poliomyelitis those referred to by Nonne, and it seems to me that Oppenheim is right in this opinion.

Eisenlohr's case[1] was remarkable on account of the limitation of the process. The weakness and atrophy affected only the right upper limb and persisted about five years. The nerve cells were degenerated only in the right anterior horn between the sixth cervical segment and the first thoracic. The white matter was normal. It is difficult to decide why this case was regarded as one of subacute anterior poliomyelitis and not as one of progressive spinal muscular atrophy.

Dreschfeld[2] regarded the case he reported as one of chronic anterior poliomyelitis. Weakness began in the right foot and leg. The tendon reflexes of the upper limbs were very prompt. The nerve cells of the anterior horns were much degenerated. Lateral sclerosis was found in the cervical region. It seems doubtful whether this should be regarded as a case of amyotrophic lateral sclerosis or as one of chronic anterior poliomyelitis.

Landouzy and Dejerine[3] did not regard their case as one of chronic anterior poliomyelitis.

A case that probably should be classed as one of chronic anterior poliomyelitis with necropsy was reported by Richard Ewald.[4]

The case that Nonne reports began with weakness in the left shoulder and left upper arm. Atrophy occurred at the same time as the paralysis or followed soon after. In the last months of the disease pains were felt in the upper part of the upper limbs and in the thighs. Nonne[5] found some degeneration of peripheral nerves, as well as of nerve cells, in the spinal cord, and he refers to the fact that in Oppenheim's case the hypoglossal and spinal accessory nerves and the nerves within muscles were not entirely normal. Nonne found atrophy of nerve fibres in the white matter of the cord, in the pyramidal tracts as well as elsewhere, but not as symmetrical degeneration.

[1] Neurologisches Centralblatt, 1882, p. 409.
[2] Brain, 1886, p. 178.
[3] Revue de méd., 1882.
[4] Ein Fall von Poliomyelitis anterior chronica, Inaugural Dissertation, Marburg, 1899.
[5] Deutsche Zeitschrift f. Nervenheilkunde, 1891, Bd. i. p. 186.

In Darkschewitsch's[1] case weakness and atrophy developed gradually in the muscles of the upper limbs, neck, back, and partly in the lower limbs. The nerve cells of the anterior horns of the cervical and thoracic regions were diminished in number, and there were numerous hemorrhages which seem to have been in the gray matter of the cord. Rarefaction of the lateral and posterior columns was observed. It is difficult to determine from the brief report why this was regarded as a case of chronic poliomyelitis and not as one of progressive spinal muscular atrophy.

In Oppenheim's[2] second case of chronic anterior poliomyelitis the weakness began in the right shoulder and right upper arm, and after a year extended to the corresponding parts of the left upper limb. Atrophy soon followed the weakness. Paræsthesia was felt in the fingers in the beginning of the disease. The nerve cells of the anterior horns of the cervical and thoracic regions were much degenerated. The columns of Burdach were also degenerated.

In the case reported by A. Dutil and J. B. Charcot,[3] the symptoms began with weakness in the upper limbs. The vessels of the cord were thickened and some small recent hemorrhages were found in the cord. This is the same case that J. B. Charcot later reported alone.

In J. B. Charcot's[4] two cases of chronic anterior poliomyelitis there was some degeneration of the anterior fundamental fasciculus—*i. e.*, of the fibres near the anterior horn. These cases possibly might be regarded as examples of progressive spinal muscular atrophy.

It is difficult two understand why Dejerine's[5] two cases should be regarded as examples of chronic anterior poliomyelitis and not of progressive spinal muscular atrophy, if a sharp distinction is maintained. In one case there was a questionable sclerosis of the interior portion of the right lateral column.

Nonne,[6] in 1896, recognized as cases of chronic anterior poliomyelitis with necropsy the two cases of Oppenheim, the two cases of his own, the case of Darkschewitsch, the case of Dutil and J. B. Charcot, and the two cases of Dejerine.

In Nonne's second case the weakness began in the shoulder muscles. The nerve cells of the anterior horns were much degenerated and rarefaction of the white matter was seen in the anterior, lateral, and posterior columns. The bloodvessels were not distinctly altered. He attributed the poliomyelitis in this case to diabetes. Nonne refers to the slight changes in the white matter observed in Oppenheim's two cases, in his own two cases, in

[1] Neurologisches Centralblatt, 1892, Bd. xi. p. 221.
[2] Archiv f. Psychiatrie, 1892, Bd. xxiv. p. 822.
[3] Le progrès médical, March 17, 1894, p. 185.
[4] Archives de médecine expérimentale, 1895, vol. vii. p. 441.
[5] Comptes-rendus heb. des séances de la Soc. de biologie, 1895, p. 188.
[6] Berliner klin. Wochenschrift, March 9, 1896, p. 207.

Darkschewitsch's case, in Dutil and Charcot's case, and in one of Dejerine's cases.

In P. Schuster's[1] atypical case of chronic anterior poliomyelitis, which was complicated by degeneration of the posterior roots and of the columns of Burdach, the patellar reflexes were much exaggerated. The explanation was supposed to be found in the slight alteration of the lateral columns.

Max Bielschowsky[2] says there are very few cases of chronic anterior poliomyelitis reported that show evidences of inflammation. In Bielschowsky's case the weakness began in the lower limbs, in the peroneal distribution, as in the case Dr. Moleen and I report. He says that contrary to the diagnosis of neural atrophy (peroneal type) were the later developments of the disease and the absence of subjective and objective disturbance of sensation. Contrary to progressive spinal muscular atrophy were the location of the atrophy, the relatively rapid development of the symptoms, and the early loss of function in the diseased muscles. Hemorrhages were found in Bielschowsky's case in the anterior horns from the lumbar to the upper cervical region. In some places the red blood corpuscles had disintegrated, blood pigment was present, and reactive processes had occurred about some of the hemorrhages. These hemorrhages were regarded as evidences of inflammation. Slight degeneration was seen in the crossed pyramidal tracts of the spinal cord as high as the pons, but was detected only by the Marchi method and was slight, exactly as I have found in the specimens studied by me. Bielschowsky observed slight perivascular round-cell infiltration and newly formed bloodvessels. The hypoglossus nuclei also were affected. This case resembles ours very closely, although the disease in Bielschowsky's case lasted nine years. The tongue was also weak and atrophied. No statement is made concerning the condition of the patellar reflex until late in the disease, when the atrophy was intense.

In Grunow's[3] case the symptoms seem to have existed about nine months. The weakness began in the right foot and peroneal palsy developed. Pain was felt in the shoulders and back. Progressive spinal muscular atrophy was excluded because the weakness began in a lower limb, because of the wide extent of the process, the implication of intercostal muscles, and the relative rapidity of development. As in our case, peroneal palsy was among the earliest signs of the disease. The pain in this case is noteworthy. Cellular infiltration was found about the arteries of the anterior fissure and about some of the vessels of the anterior horns and white matter. Necrotic foci were present in the crossed pyramidal tracts, and there were some small hemorrhages in the gray matter of the cord.

[1] Neurologisches Centralblatt, 1897, Bd. xvi. pp. 342, 392, 449.
[2] Zeitschrift f. klin. Med., 1899, Bd. xxxvii. p. 1.
[3] Deutsche Zeitschrift f. Nervenheilkunde, 1901, Bd. xx. p. 383.

The nerve cells of the anterior horns were much degenerated. Degeneration was found in the anterior and lateral columns.

Bruining[1] has observed chronic anterior poliomyelitis in father and son, and in one of the cases obtained a necropsy. In neither case were there periods of abrupt increase in the symptoms. The weakness seemed to be proportional to the atrophy. In the father the weakness and atrophy began in the right thigh and then the shoulders became implicated. In the son the atrophy began in the muscles of the neck and extended to the shoulders and upper limbs. The nerve cells of the anterior horns throughout the cord were degenerated, but no signs of inflammation were found. The capillaries of the cord were congested and in some places blood corpuscles were found in the tissues about the vessels. Bruining is not inclined to make sharp distinctions between chronic anterior poliomyelitis and progressive spinal muscular atrophy.

Rossolimo,[2] in reporting a case of chronic anterior poliomyelitis with syringomyelia, recognized that somewhat exaggerated patellar reflexes may occur in anterior poliomyelitis, and refers to the cases of Darkschewitsch and Schuster. He recognizes as cases of chronic anterior poliomyelitis only those of Oppenheim, Nonne, Darkschewitsch, Schuster (not a pure case), Bielschowsky, and R. Ewald.

Oppenheim, in speaking of chronic anterior poliomyelitis in his text-book, says exaggeration of tendon reflexes alone is not sufficient to make the case one of amyotrophic lateral sclerosis, as exaggeration of reflexes may occur in neurasthenia.

In the monograph on poliomyelitis written by Elis Lövegren,[3] the author reports a case of subacute poliomyelitis with necropsy. The weakness began in the fingers and was followed in two or three months by atrophy of the hands. The paresis and atrophy became widespread. The patellar reflexes were exaggerated. The nerve cells of the anterior horns of the spinal cord and of nuclei of motor cranial nerves were degenerated. Vessels with thickened walls were found in the spinal cord, but there was no round-cell infiltration. The white matter of the cord was said not to be involved and the pyramidal tracts to be intact. The method of Marchi was not employed. The anterior roots and peripheral nerves showed slight atrophy. A cavity in a limited area was found in one anterior horn.

Lövegren refers to two cases of subacute or chronic poliomyelitis with necropsy reported by Philippe and Cestan,[4] in which a slight sclerosis of the anterolateral columns was found; and to a case with necropsy reported by Raymond and Philippe.[5] I have not been able to obtain the paper by Philippe and Cestan.

[1] Deutsche Zeitschrift f. Nervenheilkunde, 1901, Bd. xxvii. p. 269.

[2] Neurologisches Centralblatt, 1903, p. 388.

[3] Sonder-Abdruck a. d. Jahrbuch f. Kinderheilkunde, S. Karger, Berlin, 1905, vol. lxi.

[4] XIII. Congrès international de médecine, Paris, 1900, comptes-rendus, section de neurologie, p. 271.

[5] Soc. de neurologie, Nov. 6, 1902, Archives de neurologie, 1902, 2 série, tome xiv. p. 587.

The case of chronic poliomyelitis very briefly reported by Raymond and Philippe[1] is as follows: The disease began at the age of fifty-two years in the extremities of the lower limbs, and is said by the authors to have been the first case of the kind. The antero-external muscles of the legs first showed atrophy and the weakness progressed simultaneously with the atrophy. The poliomyelitis was strictly limited to the nerve cells of the anterior horns. The anterior roots and peripheral nerves were secondarily affected. No mention is made of the employment of the method of Marchi or of the condition of the tendon reflexes.

The case observed clinically by Dr. Moleen and studied from the pathological aspect by me may properly, I think, be regarded as one of chronic anterior poliomyelitis. The commencement in one lower limb, the paralysis preceding the atrophy, the comparatively rapid development of the symptoms, the absence of sensory disturbances, and the pathological findings justify this diagnosis. The prompt tendon reflexes are unusual, but it is probable that Bielschowsky's patient would have shown the same condition if these reflexes had been observed earlier in the disease. The patellar reflexes were exaggerated also in Lövegren's case. The degeneration of the crossed pyramidal tracts in our case was very slight and perceptible only by the Marchi method. When the Weigert method was employed no suspicion of degeneration of the pyramidal tracts could be entertained. The case, however, shows that the distinctions between amyotrophic lateral sclerosis and chronic anterior poliomyelitis are not always to be sharply made. The Marchi method does not seem to have been employed in the examinations of many of the cases of chronic anterior poliomyelitis reported.

It is noteworthy that pain was recorded as present in the cases of Nonne (Case I.) and Grunow, and that paræsthesia occurred in Oppenheim's second case.

MYOCLONUS MULTIPLEX: WITH REPORT OF A CASE.

By D'Orsay Hecht, M.D.,
of Chicago,
Instructor in Neurology and Chief of the Neurologic Clinic, Northwestern University Medical School, Associate Attending Neurologist to the Cook County Institutions at Dunning, Ill.

Historical. Since Friedreich in 1881 (Virchow's *Archiv*) reported for the first time his case of "paramyoclonus multiplex," some cases similar and many more dissimilar to it have found their way into the literature under the same appellation and caused endless con-

[1] Revue neurologique, 1902, p. 1075.

fusion to clinicians and students. Little comfort has been derived from the generic term myoclonia, with which it was intended to placate every neuromuscular spasm or condition in which muscular twitching was the only or most notable symptom. It was the fate of most of the essential myoclonias reported to the number of 100 or so, after much trimming and remodelling, to neatly fit into one or the other of the many accepted forms of neuroses (tics moteur) exploited principally by the French school of neurologists. Unverricht in a retrospect of all cases of myoclonus, 48 in number, collected by him up to 1891 commented on 6 as genuine paramyoclonus multiplex; 11 looked like it, 11 others were far removed, and the rest properly belonged with the tics.

One contemporary writer of eminence, Dana, saw fit in 1903 to revise the old extensive classification whose chief merit lay in the eponymic character of the nomenclature, and I append for purposes of comparison his differential grouping:

Myoclonias and their synonyms.	Dana's grouping of myoclonias.
I. Paramyoclonus multiplex, of Friedreich; astasic myoclonia, of Vanlair; multiple spinal myoclonus, of Löwenfeld; fibrillary chorea, of Morvan; fibrillary myoclonus, of Kny.	I. Myoclonia of Friedreich, or peripheral type, including myokymia.
II. Functional, or hysterical myoclonus multiplex, chorea major, chorea electrica, of Henoch.	II. Myoclonia of the functional or hysterical type.
III. Myospasmia; memory spasm, of Friedreich; habit chorea; chorea variabile des degeneres; convulsive or spasmodic tic; tic general; Tourette's disease, myriadrit; palmus; tic neurosis, of Collins.	III. Myoclonia of the convulsive tic type, this last type being characterized by many associated spasms, choreic and tonic.
IV. Degenerative chorea, hereditary chorea. Huntington's chorea; myoclonus epilepsy; myoclonus type; myoclonia congenita of Seeligmüller (?); hereditary degenerative chorea of Sachs.	IV. Myoclonia of the degenerative chorea or "familial" or myoclonus-epilepsy type, which is closely related with the third.
V. Infectious chorea, chorea minor, Sydenham's chorea; chorea electrica of Dubini (?); chorea electrica of Bergeron; senile chorea of Gowers (?).	V. Myoclonia, of the type of the infectious and symptomatic choreas.

It is, I believe, conceded that Friedreich's classic report of this rare disease in 1881 antedated all other descriptions, and yet within a few years the literature was enriched by the records of Löwenfeld, Remak, Seeligmüller, Francotte, and Kny, followed by the views of Bechterew, Marie, Unverricht, Lundborg, Wollenberg, Boettiger, Schultze, Moebius, Oppenheim, Tourette, Strumpell, Gowers, Russel, Dana, Hunt, Walton, Clark, and Prout.

At the outset it should be made clear that one series of cases, which Unverricht elaborately described and published under the name of "Myoclonia," differed widely from those of Friedreich. Unverricht dealt with familial types and reported cases of "associa-

tion-disease" (myoclonia with epilepsy) differentiating them from the independent disorder about to be cited. I say independent disorder with some hesitation, since Wollenberg is one of those who regards paramyoclonus as a feature in the symptom-complex of hysteria; Schultze places it with the forms of convulsive tic, to which view Dana also inclines; Unverricht classes it with the degenerative choreas, and Marie, Oppenheim, Bechterew, and Strumpell, for example, favor its recognition as a disease entity.

An epitome of the Friedreich case may the better serve to show how radical have been the departures from *the original* type and how by deviation and addition the literature has grown to its present proportions and provoked such keen controversy. Friedreich tells us of a combmaker, aged fifty years, who for some time had been a hospital patient suffering from pulmonary tuberculosis. The symptoms that brought him under Friedreich's observation developed after a violent fright, which he had experienced five years before at the sight of a bursting circular saw, which accident had inflicted neither personal injury nor bodily shock. The patient was a neuropath. Two weeks thereafter he developed sharp clonic rapid twitchings in a group of muscles in the upper and lower extremities. The twitchings amounted to spasmodic contractions at close intervals, limited mostly to the biceps and triceps of both arms and the forearm supinator longus. Of the leg muscles the vastus externus and internus and rectus femoris were elected to show these clonic spasms. In the face and over the back an individual muscle would occasionally contract. Only when the spasms were especially violent were the muscles thrown into locomotion; ordinarily synergetic muscular play was not observed. The spasms varied in frequency and intensity. The movements abated during sleep, but mere resting in bed had the effect of increasing them to even tetanizing strength. Work or voluntary movements brought the spasms under almost complete control. The dynamic motor power was not impaired—the electrical reactions remained normal; there was no idiomuscular swelling, so-called myoidema, upon stroke of the muscle volumen with the hammer. Cutaneous irritation, however, produced excessive muscular spasm. The patellar tendon reflexes were markedly exaggerated. The mental state was absolutely sound; pupils negative; all physical functions normal except for headaches and dizziness. Galvanization at frequent intervals led to a decrease in all symptoms and the patient was given his discharge shortly after.

Hunt[1] comments on the Friedreich case as follows: "The peculiar features of this affection—viz., the spontaneous contraction of individual muscles not singly under the control of the will, and the absence of the synergetic muscular action in the affected members,

[1] Journal of Nervous and Mental Disease, July, 1903.

were so at variance with the known characteristics of muscular contractions of cerebral origin as to render some other explanations probable. Friedreich, after a careful consideration of all the possible sources, as the brain, spinal cord, nerves, and muscles, proposed the hypothesis which referred the symptoms to an *excessive irritability of the anterior horn cells of the cord.* This theory was in harmony with the special clinical features of the case—*i. e.*, the single muscle contraction, the absence of synergetic action, the great exaggeration of the knee-jerks and their diminution as the motor symptoms subsided, the great susceptibility of the contractions to the peripheral stimuli and their cessation on voluntary innervation of the part."

PATHOGENESIS. More regrettable than the confusion which has arisen concerning the classification of this affection is the speculative attitude toward its origin.

Friedreich sought to locate the lesion for this unusual symptom-complex in the spinal cord, and although the weight of the evidence still favors this view, Hunt feels that pathological anatomy has thrown no positive light upon the subject. He infers this much from the negative results obtained after thoroughly conducted histological examinations in two cases, one investigated by Friedreich and the other by himself. In the original Friedreich case Schultze's examination of nervous structures and muscle tissue (the biceps) was entirely negative. Hunt's finding of a normal cord in his case of similar clinical type was equally disappointing, but he fared somewhat better in his study of the muscle fibres, which were found to be greatly hypertrophied and showing sarcolemma nuclei between the sarcous elements. In speaking of their presence Hunt says: "This is a peculiarity of the so-called red fibres of the lower vertebrates, a form of muscle which is more active and capable of more prolonged contraction than the white fibres, which constitute human muscle, although such red fibres are scattered in very small number throughout the muscular system in man." The thought that excessive and long-continued muscle twitchings and spasms could account for the muscle hypertrophy was dismissed when comparison was made with a slide of muscle tissue from a chronic progressive chorea of fifteen years' duration, in which the fibres were normal.

Neither in the protracted spasmodic conditions of cerebral origin nor in the class of muscular dystrophies and hypertrophies are such changes in muscle noted.

In an attempt to correlate Friedreich's theory of the possible spinal origin of the disease with his own observations of muscle change, Hunt concludes that a trophic relation may be responsible, thus strengthening the conviction in favor of cordal disease. That the anterior horn cells exercise a trophic influence resulting in atrophy of muscle is taken for granted when Hunt says, "it is

reasonable to assume the possibility of an increased trophic function with resulting hypertrophy."

The view of a cortical origin of paramyoclonus is more especially held by those who have been privileged to study the tissues of those rarer cases of paresis, chronic meningitis, and epilepsy associated with myospasms throughout their course. In an article entitled "Del Paramioclono Molteplice" Murri expressed the conviction, based upon 3 cases observed and autopsied by him, that disease in the Zona Rolandi, which he did not always succeed in finding, may and does give rise to polyclonus. There is something unsound in an argument that insists on the existence of a disease focus when all determinable evidence thereof is lacking.

Introductory to their paper on "The Nature and Pathology of Myoclonus Epilepsy," Clark and Prout say of essential myoclonus (paramyoclonus multiplex), "our knowledge of the pathological seat of essential myoclonus, while still defective, is tending more and more to place it in the cerebral cortex, where most other chronic convulsive disorders are being located. We have no doubt that even the milder types of essential myoclonus when studied in the light of more recent and definite histological changes of the cortex from cases of myoclonus epilepsy (the most marked and fatal form of the myoclonus) will disclose its pathogenesis to be in those cortical elements of the third or pyramidal layer and will show that the lesions belong to that form of cell degeneration which is so uniformly present in the second layer cells of the epileptic brain. If such findings prove true in a large number of cases of essential myoclonus the disease must be classed as an affection similar in pathogenesis and course with that of epilepsy; or, in other words, that there exists a soil of degenerative predisposition upon which is engrafted an autotoxic excitant."

Clark and Prout share with Unverricht in this somewhat positive assertion of a cortical origin of the disease and their deductions are made from the premises of myoclonus epilepsy. In reflection of the enormous number of cerebral cases in which small and numerous pathologic foci are found identical with those seen in myoclonus epilepsy, it is not far-fetched to ask why we do not see intravitam more of these twitchings and spasms of the paramyoclonus type. They are genuinely rare in the symptom complex of the many brain states whose underlying pathology is well understood. It may be safely contended that the myospasms associated with cerebral disease are not at all of the paramyoclonus type. They are neither so violent nor so rapid nor confined to individual muscles nor so widely distributed. They resemble the more coordinated movements of the average tic.

Experimental study has thrown little or no light on the subject. A muscle does not respond individually to an electrode be it applied ever so carefully to the motor cortex. The response is one of move-

ment of a group of muscles. Hunt states that Sano's experiments have a better hearing on this point and go far to demonstrate that the individual muscle is represented in the anterior horn cell.

Moebius regards paramyoclonus as an hysterical manifestation, and Dejerine, although less positive in that assertion, thinks it has much in common with familiar motor symptoms of hysterical nature.

In citing the following case I beg to remark on its clinical agreement with Hunt's understanding of myoclonus multiplex, "a term which should be reserved for that form of myospasm characterized by multiple spontaneous, isolated contractions of individual muscles."

A. W. P., a male, aged twenty-eight years, six feet tall, weighing 180 pounds, and by profession a prize fighter, was admitted to the neurologic service of the Cook County Institutions at Dunning January 1, 1905, and was there seen by me for the first time in April of same year.

Family History. Except for the fact that his father, who had always been a heavy smoker, died of a cancer of the lip at fifty-two, the patient's antecedents prove uninteresting. His mother is living and perfectly well at fifty-eight. Two brothers, one a pugilist the other a "buck dancer," enjoy good health, and of his two living sisters he has no knowledge.

Previous Illnesses. The patient states with much positiveness that prior to the onset of the present illness he had never known a sick day. Inquiry into his venereal history brings a confession of three attacks of gonorrhœa, but a local sore is stoutly denied and constitutional evidence of past syphilis is lacking.

His personal habits have been outrageously bad. As he says, "when not fighting men he was fighting booze." For fifteen years he has been a heavy drinker of hard liquor, and his sexual indulgence, following several years of rather pernicious masturbation, has been excessive. He has passed through all the vicissitudes that go with his chosen profession.

Present Illness. In the fall of 1902, in company with some fellow-fighters and trainers, he became as he calls it "paralyzed from drink." A party of four men consumed seven quarts of whiskey at one sitting. It was directly after this "drunk" that he felt and saw a twitching, "a jumping" of the abdominal muscles, which in the course of a few weeks had spread so as to have affected all the muscles of the trunk. Simultaneously fine muscular contractions appeared in the left hand and arm, rendering it too unsteady to be of any service. Careful inquiry fails to reveal the fact of a regular progression in these twitchings; they seemed universal, and in January, three months from date of onset, they had attained the dignity of spasms severe enough to make walking impossible.

Drink was necessary to steady his gait throughout the winter months of 1903. He had quit fighting altogether and devoted his

time to the training of other pugilists, punching the bag, drinking, and sporting. In the spring of 1903 he did odd jobs at a race-track, principally walking horses for exercise. During the summer he lived in out-door camps, and the following winter kept himself well enough under the influence of liquor to do snow-shovelling. The early part of 1905 was spent in Detroit, where he got sixty days for drunk and disorderly conduct.

At the time of commitment his spasms were so generalized and severe that he could not walk. Only by sitting down and shoving himself along could he move about. Throughout the entire illness there has never been a complete let up in the spasms. He states that occasionally days intervene when "the jumps" are milder and enable him to walk or stand, but the "hard spells," to use his phrase, may persist for days, weeks, or months without the slightest variation in intensity. At times he experiences hard, dull pain in the lumbar region and across the shoulders.

It would seem from what he says that the hardest spells are preceded by prodromata, described thus: A bright zig-zag light flashes before one eye, the right only, compelling him to lie down immediately; then follows a very intense frontal type headache, which only succumbs after indulgence in food or drink. His nerves then quiet down to a state of what he calls "ordinary spasms." He has never experienced symptoms that even remotely resemble an epileptic fit. There has never been loss of consciousness, frothing, biting of the tongue, bed-wetting, or tonic rigidity. Emotional excitement aggravates the spasms. Will power exercises no control.

Status Præsens (objective findings). The man presents a physique which attests to muscular development and power. The many batterings which his face and lips have received in the course of a fistic career and the flattening of the nose from repeated fractures lend a rather unlovely expression to his features.

It does not require the removal of clothing to note the lightning-like jerks that play through the various muscles of trunk and extremities, and every now and again become so severe as to give the impression of his being thrown from the chair to the floor. The muscle contractions impress one as being induced under the stimulus of an invisible electrode. So severe and shock-like are the seizures that locomotion is well-nigh impossible. Any effort at standing, even though supported, meets with difficulty from the violence of the spasms. The act of dressing and undressing is most tedious and cumbersome, since all attempted movements seem to aggravate to greater helplessness.

Resting in bed with all clothing removed, the generalized clonic seizures present a most unusual picture. In parts of a muscle one sees a faint quivering of a few fibrils. In a larger muscle, the fascicular type of twitching is evident; then again muscles singly or in groups spring forward in sharp tetanic contractions, while still

others are so clonically convulsed that locomotor effects result. Here, there, everywhere, together or in rapid succession, the play of muscles goes on. During one extremely severe spell, which I witnessed, no muscles seemed spared; even the muscles of the eye, the tongue, and the occipitofrontalis were observed to share in the seizures. With the examining hands placed on the peroneal flexors of both legs at the same time the "tic" was distinctly appreciated on the left a second before it was felt in the right. Very close watch with the eye confirmed this succession. The tic appears bilaterally symmetrical, but is not bisynchronous. The entire left side is much more affected than the right, justifying the use of the term hemiparamyoclonus. Bernhardt has described a case of hemimyoklonia.

In the left leg muscles everywhere it was noted that a few minor tics both palpable and visible precede the major spasms, most of the latter being severe enough to throw the limb off the bed. On timing the larger seizures it was shown that they recurred about every three or four seconds and the slower minor twitchings occurred in the intervals about one second apart. Since the left-sided spasms are greater by far than those of the right, the motor effect is correspondingly greater and the left side the more helpless of the two.

The contractions everywhere were clonic, never tonic, and it would be impossible to declare any muscle or set of muscles free. The face, trunk, and periphery are alike the seat of constant spasms. The muscles chiefly involved are the deltoids, pectorales, flexors, and extensors of the legs and arms, the gluteals, abdominal, back, and thoracic muscles, as well as those of the diaphragm. Everywhere the rapidity and the intensity of the spasms varied. In the face their fibrillary character could be beautifully detected in the small muscles, the risorius and buccals. In the glutei a short wave could be distinctly seen and felt, and here the tic seemed slower, more rhythmical, reacting more like a muscle that shows a slight R. of D. to the faradic current; its bilateral character was more readily observed. In the brief absence of large clonic spasms, the fine fibrillary twitchings persisted even the small musculature of the feet and in isolated muscles that are not under control of the will. Hunt has observed this peculiarity in a case observed by him and commented on the isolated contraction of the supinator longus and sartorius muscles, which cannot be operated at will. Over the right pectoral the myospasm caused the muscle to form in a lump-like mass.

The speech of the patient is, from the combined force of a diaphragmatic and laryngeal spasm, too interrupted and explosive to be understandable. Before the patient could speak with a semblance of comfort he had to be given whiskey and chloral. With every severe seizure involving these muscles there is a loud inspiratory grunting sound as if the patient were choking. Deglutition is often a two-step or three-step act. Upon being given a slice of bread

to eat the spasm held a piece of it in the back of the throat, releasing it after a few seconds and so enabling him to complete the act of swallowing. The same sensation obtained in the act of drinking.

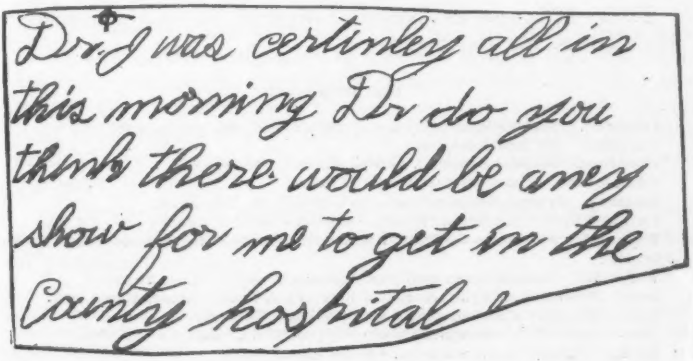
Bladder and rectum had never been incontinent nor disturbed, and the sexual power remains normal.

The muscular system is well developed, nowhere showing a pathological degree of atrophy or hypertrophy. Motor paralysis is absent and such disability as exists is entirely borne of the myospasms and the paresis or reduction of dynamic power can readily be attributed to disuse. The dynamometer registered 100 with the right hand and 70 with the left. *Myotatic* irritability is increased. Stroking the soles of the feet caused a notable increase in the twitching. An electrical examination was not made. The tendon reflexes everywhere are brisk, especially the jaw and knee-jerk. The Babinski toe sign was absent. The cremaster was well marked. The eyes are normal, the pupils react properly. The frontal eminences were unduly prominent. Sensation was nowhere disturbed.

The patient states that he feels better in the afternoon than in the morning. Lying on the left side is next to impossible, and keeping on his back is an equally great hardship; he gets only comparative comfort in any position, but favors lying on the right side. When first taken ill, he found that though bedridden by day, he could walk some at night, an anomaly which does not obtain now.

Despite this body and nerve-racking affliction the patient is uncomplaining, unemotional, and rather inclined to be witty. He has not suffered the least impairment of his mind.

I append an extract from a letter written by the patient while under control of whiskey and such irregularities in the tracing of letters as would be expected, nor does the up or down stroke show even so much as heavy shading from undue pressure in steadying the hand for the task. Free from the influence of whiskey writing is utterly impossible, as are all other acts of the will.



TREATMENT. During an all too brief period of observation several hypnotics and sedatives were tried and in nearly all instances with indifferent result. Sulphonal in 30-grain dosage given in hot milk and repeated in two hours had the effect of only slightly reducing the twitchings. Sodium bromide and the combined bromides in dosage of 1 to 2 drachms and upward failed to induce quiet, much less sleep. Hyoscine hydrobromate ($\frac{1}{150}$ gr.) hypo. had absolutely no effect on the spasms. Morphine sulph. ($\frac{1}{4}$ gr.) hypo. was equally inert. Choral in 10-grain doses by mouth had a quick sedative action where all other drugs failed, and 20 grains subdued the contractions for several hours. Better than all these in its sedative action was whiskey in 1-ounce doses. Given alone it would steady patient in about thirty minutes and make walking, writing, and eating an easy matter. Alcohol *added* to any of the drugs mentioned acted beneficially when the drug alone proved useless.

In Dana's case alcohol was without the least effect and I note what Clark and Prout say of various remedies used in their myoclonus epilepsy cases, "Alcoholic excesses usually excite a series of myoclonic contractions, yet small amounts of alcohol often markedly diminish the myoclonus for a time." Of chloral they say, "when given alone it has but little power in checking the myoclonic contractions and is practically of no value in diminishing the frequency or severity of the epileptic seizures."

A half-pint or pint of whiskey, which the patient on one occasion was allowed to consume in a half-hour or less, steadied every nerve and muscle in his body for almost an entire day. To sum up, then, whiskey or chloral or both proved to be the only successful agents at my disposal for allaying the myospasms. The diet and general hygiene were such as fall to the lot of patients in a large county institution. The patient was discharged unimproved on June 1, 1905, and immediately repaired to his home in Detroit.

I am indebted to Dr. Swan, senior physician at Dunning, for the use of some of his notes.

N. B.—The case was presented (in brief) at the May meeting of the Chicago Medical Society.

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INFECTIOUS ARTHRITIS: A BACTERIOLOGICAL CONTRIBUTION TO THE DIFFERENTIATION OF THE "RHEUMATIC" AFFECTIONS.

By Roades Fayerweather, M.D.,
CLINICAL ASSISTANT IN ORTHOPEDIC SURGERY, THE JOHNS HOPKINS HOSPITAL, BALTIMORE, MD.

(From the Orthopedic and Pathological Laboratories of Tufts College Medical School, Boston.)

I. Introduction.

It is surprising, considering the frequency with which "rheumatic" joints of unknown origin, and not referable to commonly accepted types, are met with in any general hospital or similar private practice, that so little is known of the actual etiology in this large group of cases.

The report here presented deals particularly with three cases of this nature in which the bacteriological findings have appeared of sufficient importance to warrant consideration in detail. The fourth case is one of typical acute articular rheumatism. In order to show their relationship, clinically and otherwise, with rheumatic disturbances in general, I wish to refer briefly to that classification of rheumatic joint affections which seems best to accord with our present knowledge.

CLASSIFICATION OF RHEUMATIC AFFECTIONS.

Exclusive of simple traumatic cases and of suppurative conditions of pyogenic or mixed bacterial origin, the term *rheumatic affections* is here used broadly to include cases in which joint symptoms form a more or less prominent feature.

1. Tuberculous and secondary syphilitic joints find a place here, as do also certain arthritides in which a specific bacterial cause has been determined—gonorrhœal, pneumococcic,* etc. Here, too, though with less certainty as to their exact nature, we may include joint involvements directly following specific infections elsewhere in the body[1] [2]—typhoid fever, scarlet fever, measles, dysentery (Shiga's), influenza.

2. As examples of arthropathies of nervous origin may be cited those of tabes, syringomyelia, neurasthenia, and of certain cases of peripheral neuritis.

* The majority of pneumococcic joints, however, proceed to suppuration. Cave, in Lancet, January 12, 1901, has reported thirty-one cases collected from the literature up to that time, nearly all suppurative.

3. The articular disturbance following administrations of diphtheria antitoxin illustrates cases of toxic origin.

4. Another class of cases may be attributed to hereditary and diathetic conditions—*e. g.*, those seen occasionally in hæmophilia. Gouty joints, both the acute and the so-called chronic types, have been variously classed as toxic or as diathetic.

This would account for practically all the sharply acute inflammatory conditions except those we are accustomed to designate as the acute articular rheumatism occurring in rheumatic fever. Reference will be made later to the claims of this condition to classification with the infectious arthritides.

5. Beside these there yet remain several other conditions which have been reserved to the last because of the great confusion and disagreement that has followed attempts to differentiate them; for this reason Osler and others have preferred to consider them collectively under the name of *arthritis deformans*. In this group it is probable, in the light of recent work, that we have to differentiate at least two distinct classes of cases—those in which *changes of an essential nature occur in the bones and cartilages* of the joints involved, and those in which *such changes are absent or are secondary* to the primary lesion. It seems possible that these two classes are also etiologically distinct, and that the latter are of infectious origin.

It is to this latter class that my first three cases belong. In referring to it I shall use the name first applied to it by Schüller[3]—*infectious "polyarthritis chronica villosa."* It will be more profitable to examine at once the character of these cases themselves before discussing the propriety of grouping them with others under the head of *arthritis deformans*.

INFECTIOUS POLYARTHRITIS CHRONICA VILLOSA.

Clinical Characteristics. This is an affection which may develop at any age, in infancy or in adult life. Marantic conditions predispose to and often definitely introduce it. It follows sometimes upon parturition. A varying degree of constitutional disturbance may mark the onset, though this is often entirely absent and the first symptoms may appear in the joint without any assignable cause. With little or no warning a joint may become sensitive and quickly exhibit signs of an acute inflammatory nature. The local picture at the onset is so similar to that in rheumatic fever that it needs no description. As in the latter condition, several joints are generally attacked in rapid succession, as a rule the larger articulations, though the small joints of the hand are frequently involved as well. The local symptoms are usually milder, but may approach in severity those of rheumatic fever. Some enlargement of the neighboring glands is not uncommon. A moderate leukocytosis is the rule in the early stage; the pulse rate is almost invariably high

(95 to 110) in adults, but there is generally little or no pyrexia. The heart is rarely affected; chorea and subcutaneous nodules* have not been noted.

So far there is little to distinguish these cases from mild forms of rheumatic fever; their *subsequent course*, however, is very different.

In the latter condition the course throughout is essentially acute, the *restitutio ad integrum* of the joints being rapid and characteristic. Directly the opposite is true of the class of cases in question. With frequently no interference with the general health the course is protracted, and the acutely inflamed joints of the early stage acquire a chronically congested and much hypertrophied synovial membrane which permanently deforms the joint. Recurrences of the acute condition after intervals of comparative quiescence are characteristic. From continued disuse shrinkage of the capsule may occur, and contractures of the surrounding muscles, eventually, though rarely, leading to true bony ankylosis, but the entire absence of essential lesions of the bone or cartilage sharply distinguishes it from the *atrophic* or *hypertrophic arthritis* of Goldthwait.[2] Chronic hydrops may continue to be a feature for a longer or shorter period; it is of the character of a transudate, never, apparently, exudative. When the process has not been unusually protracted so that contractures have occurred, the only interference with function is that presented by the hypertrophied synovial folds which act as foreign bodies in the joint. As in other conditions in which such villi are developed it frequently happens, however, that these become adherent to various portions of the synovial walls, and unless proper attention be given to breaking up such adhesions a permanent disability may result.

Pathological Characteristics. The examination of such joints after characteristic changes have developed shows a condition of villous hypertrophy of the synovial membrane. The character of the tissue varies considerably with the stage of the disease—in the recent cases frequently showing marked turgidity and congestion, later often acquiring a comparatively anæmic character. The histological picture varies accordingly. The occurrence of obliterating endarteritic changes may cause necrosis, with rupture of the pedicle and production of joint-mice. Occasionally a general synovial thickening takes place and definite villi are absent. After sufficient quiescence lipomatous transformation of villi is not uncommon; metaplasia into bone or cartilage is observed fairly frequently, and at other times deposits of amorphous lime salts. The fibrous capsule is generally thickened.

Very similar changes are produced in a variety of other conditions, due to local inflammations from various causes. Interest-

* Though mentioned by Bannatyne (Rheumatoid Arthritis, 1898, p. 74) it is uncertain as to what class of cases he there refers.

ing as these are, their consideration here is not to the point. Painter and Erving[4] have discussed the subject at some length, and with numerous references to the work of others. Schüller,[5] in 1900, in the course of a series of communications, described the histological differences in the synovial villi produced in various conditions, illustrating with cuts.

Compared with the *histological* picture presented by these other villi of various origins, it may be said of those arising in *infectious polyarthritis chronica villosa* that they differ from the former in showing a more extensive thickening of the synovial membrane and a tissue of more cellular character. Moreover, the character of the cells themselves differs with some constancy, for in addition to the large fixed cells with large, clear, vesicular nuclei which, together with their supporting framework of branching fibrous trabeculæ, form the structural background in almost all villi, we see here numerous plasma cells, and a disproportionate increase of infiltrating small round cells, and, in cases where the process is still active, great numbers often of polymorphonuclear leukocytes and eosinophiles. The lymphoid cells appear particularly as a continuous zone beneath the free surface, but nodular aggregations of considerable size are often met with in the deeper layers, especially about the numerous bloodvessels. The lymph channels are large and abundant. The free endothelial border of the synovial membrane often shows several layers of cells instead of the normal, single, flat layer.*

The histological picture is always beautiful. Though moderately characteristic in certain stages, it can never, of course, be relied on as in any way of diagnostic value. The gross anatomical picture is of more value, but it is the clinical features that are of chief importance. As to the value of the *x*-ray picture in the differential diagnosis from *atrophic arthritis* Goldthwait[3] speaks positively.

It is not my purpose to describe these cases further than will suffice to illustrate clearly the class with which we have to deal. It must be added that clinically they may display very considerable variation from the general type outlined above, *all characterized, however, by a course of a chronically infectious nature, polyarticular, with the production of permanent changes in the joints, affecting primarily only the periarticular structures, and having little or no tendency to display lesions elsewhere in the body.*

Relation to Arthritis Deformans. Nomenclature. It is necessary for the sake of clearness to touch briefly on this subject. Of the many terms applied to certain chronic deforming diseases of the joints, the most commonly used in this country is *arthritis deformans*, and it is just as well to disregard the numerous other terms synonymously employed.

* In one case (synovial villi removed from the wrist-joint in a case that had presented typical clinical and pathological features) the cells of the free border had acquired a cuboidal form.

Osler's classification is probably the best known. His subdivisions under this head are: (1) Cases with Heberden's nodes; (2) general progressive arthritis—polyarticular, and occurring both as acute and chronic forms; (3) monarticular forms; (4) vertebral —spondylitis deformans; (5) Still's disease.

Goldthwait, on the other hand, makes but three subdivisions, based rather on the pathology and supposed etiology. These are: (1) Hypertrophic arthritis*—including Osler's subdivisions (1), (3) and (4), characterized by essential hypertrophic changes in the bone, supposedly due to disordered metabolic conditions. (2) Atrophic arthritis, including cases of similar nature, characterized, however, by primary atrophy instead of hypertrophy, the changes first appearing in the articular cartilage and thence extending to the bone—it is evident that only part of Osler's subdivision (2) belongs here. (3) Infectious type, including the remainder of Osler's subdivision (2), together with all cases of Still's disease. The latter are included here in the belief that they are merely manifestations in childhood of the same conditions, Still having described only the most striking —*i. e.*, the fatal cases.

This last subdivision of Goldthwait's is identical with the class of cases I have called *infectious polyarthritis chronica villosa*. As these cases differ clinically, pathologically, and probably etiologically† from the hypertrophic and atrophic types there appears good reason to restrict the application of the term *arthritis deformans* to the latter two forms, which have important features in common. Goldthwait retained the "infectious type" under the general head, apparently as a concession to our usually accepted classification, to avoid confusion, and for lack of definite proof as to their etiology. Of more significance is his mention of this same class of cases in his article[2] entitled "Infectious Arthritis" (pp. 6 and 8).

Henceforth in speaking of *arthritis deformans* I shall have reference only to the cases of the hypertrophic and atrophic types.

The name of Max Schüller, of Berlin, deserves mention with this group of cases, for his is the honor of being the first to distinguish them as such. This he did first in a paper[3] presented to the XXI. Cong. der Deutsch. Gesellschaft f. Chir. in 1892.

Again,[3] in 1897, he differentiated them clearly from cases of *arthritis deformans* by the absence of essential changes in the articular structures proper, but was unwilling to commit himself as to their exact relation to ordinary acute articular rheumatism. His report was based on the observation of 56 cases. The condition

* In his earlier writings Goldthwait distinguishes *osteoarthritis* and *rheumatoid arthritis*. These terms are synonymous with *hypertrophic* and *atrophic arthritis*, which were subsequently adopted as being more accurate and less confusing.

† McCrae (Journal of the American Medical Association, October 8, 1904) states his belief that all three forms are of infectious origin, but there is no scientific evidence in support of this. As to the work of Bannatyne, which is supposed to favor this view, reference is made later.

he termed "*polyarthritis chronica villosa*," and distinguished two types: (1) with chronic capsular thickening and great synovial hyperplasia, resulting in a greatly deformed joint with marked limitation of motion and persistent pain; (2) with capsular atrophy and villous formation limited to only a small area, pain a feature as above. As to his bacteriological findings I shall have occasion to speak later on. His descriptions are brief and clear, and are worthy of examination.

Subsequent observers, especially in England,* and certain writers in this country have referred to Schüller's work, but have failed to recognize the truth of his distinctions, and have confused his cases and their own with forms of true arthritis deformans. Thus, in reviewing the literature with reference to the special group of cases in question, it is always necessary to take into account the clinical and pathological features of the reported cases, and to disregard the various terms according to which their observers have classified them.

Speaking of the same group of cases distinguished by Schüller, Goldthwait[2] writes: "It is also possible, and indeed probable, in the light of recent reports, that organisms have been found, or will be found, which will explain some of the cases which, up to the present time, have been shown to be undoubtedly infectious, but in which the definite organism could not be found." These words may well serve as an introduction to the following report:

II. Report of Cases.

In the collection and disposition of the materials used for bacteriological purposes particular attention was paid to avoiding contaminations.

CHANCES OF ERROR. TECHNIQUE.

This is mainly a consideration of the opportunities and possibilities of contamination. Where *aspiration* is employed there are three special sources of danger.

(*a*) Contamination from the *skin*. It must be conceded that this is possible, though reduced to a minimum by suitable preparation of the patient. In all my cases the parts were prepared as for a major operation, in most of them a bichloride poultice was worn for the preceding twenty-four hours. The organisms cultivated are not such as we recognize as the ordinary inhabitants of the skin.

(*b*) Contamination from the *air*. It is but fair to draw attention to this ever-present source of error. All manipulations were planned with reference to avoiding this. The syringe, after sterilization,

* The recent references by W. Hale White, and by A. E. Garrod to this group of cases are, however, definite. Lancet, March 18, 1905.

remained covered until required; it was handled with properly disinfected hands, and care was taken not to touch the needle itself. Inoculation of tubes was made at the bedside, plugs and mouths of tubes well flamed, and transfers carried out as rapidly as possible.

(*c*) Contamination from the *syringe*. This was avoided by using an instrument all parts of which could be boiled, being entirely of glass with the plunger wrapped with asbestos, and with a stiff rubber connection for the needle. These were boiled for fifteen minutes before using, and resterilized before aspirating a second joint of the same patient.

Cases in which material was obtained at *operation*. Contamination from the *air*. This is practically the only source of error here. My practice has been to have on the table, covered in the bag in which they were boiled, a graduated glass of suitable size and a small glass funnel. Before opening the capsule, and after bleeding is well controlled, the glass is taken from the bag and held close to the capsule, the wound being well retracted. The capsule is then nicked and contents allowed to escape into the glass.* The latter is at once covered with a fresh sterile towel that has not been exposed to the air, and as soon as possible the contents are rapidly transferred to a sterilized, cotton-plugged flask, the small funnel being used for this. If sufficient fluid is not obtained cultures are made directly from the joint on blood-serum tubes, and smears are likewise prepared. Any bits of tissue removed from the joint are at once folded between sterile sponges that have not been exposed to the air.

Notwithstanding all these precautions there remains, theoretically, a considerable chance for contamination. That this will seldom occur is shown: first, by the larger number of cases in which no organism was cultivated; secondly, by the consistent results obtained in the other cases where the same organism grew in pure culture in tubes inoculated from different joints of the same patient, or in tubes inoculated separately with the fluid, and with the tissue from the same joint. In the case of rabbits, where chance of contamination is much greater, it is worthy of note that out of thirty-nine aspirations from which cultures were attempted, all either remained sterile or yielded in pure culture the organism injected, excepting two tubes which were contaminated.

From 9 cases of various clinical types cultures from the joints were attempted on blood serum. Of these only 4 gave positive results. The negative cases were as follows:

Negative Cases.

No. 5. Mr. M. (Corey Hill Hospital, Dr. Goldthwait.) *Atrophic arthritis* (many joints). All cultures remained sterile. They were

* Dr. Leary has suggested a much simpler and safer method—viz., the aspiration of the fluid through the capsule after the skin incision is made.

taken from the knee-joint fluid obtained by aspiration, and later at operation, and numerous tubes were inoculated. The attempt was also made to grow cultures in large quantities of bouillon after Blaxall's* method. Three blood-serum tubes were also inoculated with bits of snipped-up synovial tissue from a small quantity removed at operation. No organisms were seen in smears fromthe fluid.

No. 6. Miss H. (Carney Hospital, Dr. Painter.) Considered to be an early *atrophic arthritis*. An afebrile polyarthritis with acute pain and slight effusion in left knee-joint. At time of aspiration the effusion had practically disappeared, but a few drops of clear fluid were withdrawn from the left knee-joint and two plain blood-serum tubes and one blood-smeared tube inoculated. The two plain tubes remained sterile, the third tube was doubtless contaminated. Smears from needle-point negative.

The culture medium in the third tube was blood serum that had been smeared with placental blood (collected aseptically and kept on ice in Ehrlenmeyer flasks). A number of such tubes were prepared and incubated for several days before use, but as many which were not used, but remained in the incubator, developed growths after a longer period (seven to ten days), no cases are reported as positive in which this medium was used.

No. 7. John W. (Carney Hospital, Dr. Painter.) *Infectious arthritis following influenza.* This was a comparatively recent elbow in which, however, synovial fringes had developed and proliferation had been stimulated in the head of the radius. Cultures were made from the synovial fluid, which, though thick and syrupy, was clear and but slightly in excess. Bits of synovial tissue, and bone removed from head of radius were also placed in separate tubes of the blood-smeared serum. No growths were obtained save such as were clearly contaminating. Smears from synovial fluid negative.

No. 8. Arthur L. (Carney Hospital, Dr. Minot.) *Acute articular rheumatism.* This was a first attack, in both wrists and knees and in one elbow, with mitral insufficiency. The arthritis subsided quickly and at time of aspiration only a drop or two was obtained from either knee-joint. Blood-serum tubes inoculated, but remained sterile; smears from needle-point negative.

No. 9. Miss A. (N. E. Baptist Hospital, Dr. Goldthwait.) *Chronic infectious arthritis* (many joints). This represents the border-line cases, in which, though of evident infectious origin, and without essential bone or cartilage involvement, permanent peri-articular change has been produced, without, however, well-marked villous proliferation. It seems likely that subsequent attacks might produce the typical picture described by Schüller.

* Lancet, April 25, 1896. It was realized, however, that the cases with which Blaxall worked, though described as "rheumatoid arthritis," were undoubtedly not of the atrophic type, but of the variety differentiated by Schüller.

The left knee-joint was aspirated under cocaine anæsthesia, with rigid aseptic precautions, and three or four drops of fluid obtained. Two tubes were inoculated, one of plain and one of blood-smeared blood serum. Smears from needle-point negative. Two days later a pure culture was discovered on the plain tube—a motile, pale-staining bacillus, decolorized by Gram's. The organism grew in discrete, round, elevated, colorless colonies, not visible to the naked eye until the third day; when fused, indistinct granular patches appeared. It was very difficult to obtain smears, apparently from unusual coherence of the organisms, and the firm, membranous-like character of the colonies, so that it was necessary to pick a colony up bodily and crush it on the slide; even then few isolated organisms were found compared with those that remained *en masse*. Sub-cultures on fresh blood serum developed slowly, the colonies later acquiring a yellowish hue.

On the second day after aspiration the blood-smeared tube also showed a growth similar in character to that described, but because of inability to obtain the organism in smears the colonies were regarded as perhaps oil-droplets or something else extraneous, unlikely as this appeared. A subculture on fresh serum was attempted, however, and yielded a pure culture from which smears were successfully made, showing presence of the same organism above described from the original—not the parent—tube. This organism was not of the character of the contaminating cocci that grew on many of the blood-smeared tubes. Moreover, it was found in pure culture on *both* the original tubes, one of which contained plain blood-serum. Nevertheless it is thought unfair to include it with the report of positive cases, although of sufficient interest to warrant consideration because of its similarity in certain respects to the spore-bearing organisms isolated in three of the positive cases. Besides it bears, so far as studied, a considerable resemblance to Schüller's and Blaxall's bacilli. It is hoped that another opportunity may be offered to study this case.

Positive Cases.

Case I.—Frank A. L., Massachusetts; aged twenty-eight years; machinist. Admitted April 27, 1904. Carney Hospital, orthopedic service, Dr. Painter.

Complaint. Stiffness of various joints; persistent swelling in knees.

Family History. No tuberculosis, neoplasm, or joint affections.

Personal History. Gonorrhœa at age of eighteen; no complications. Measles at age of twenty-four. No history of chronic diseases (except of joints), chorea, or any nervous disorders. General health always good. No history of traumata or surgical operations.

Joint History. At age of seventeen, eleven years ago, developed moderate pain, with stiffness, in both hips; onset sudden, preceded

by chill, following exposure to cold and wet; not in bed, but off feet for two to three weeks; no subsequent attack in hips. For past four years has noted moderate tenderness about shoulders, with some stiffness in those joints. One year ago, April, 1903, having gone to bed in excellent health, woke with severe dull ache in both knees; considerable swelling, but no redness or heat. Condition continued unchanged for four months, not preventing work; since then knees have remained swollen, but painless, excepting on attempting to use joints after some inactivity. Eight months ago noted stiffness, without pain, developing in neck. Appetite good; sleeps well; bowels regular.

Physical Examination. Poorly developed, emaciated, pale. *Chest* symmetrical; expansion (across nipples) limited to 1.5 cm. *Lungs* negative. *Heart* of normal size and position; both sounds clear; at the apex a soft systolic murmur, faintly transmitted to the axilla, not heard in back. *Abdomen* negative, spleen and liver not felt. *Glands:* moderate, soft enlargement of posterior cervical, right axillary, and both inguinal groups. *Reflexes:* knee jerks present and equal; ankle clonus fairly distinct on left; no Babinski.

Special Examination. Spine: Stands with considerable list to the right; back shows a long, gentle kyphotic curve, of postural variety, with a double scoliotic curve, and no apparent rotation; cervical spine slightly flexed forward; practically no motion whatever permitted by spine, except to a slight degree in cervical region. *Shoulders:* rotation free; all other motions much restricted. *Elbows, wrists, hands,* negative. *Hips:* habitual slight flexion and abduction hips very stiff, but with some manipulation, flexion, abduction, and adduction can be carried to almost normal limits; rotation about one-half normal; symmetrical atrophy of both thighs. *Knees:* both are symmetrically enlarged throughout the synovial outlines of the joint; no redness or heat; not sensitive to palpation; patellæ freely movable and do not float; swelling feels boggy and soft, irregular masses can be felt to glide under the examining fingers; no bony thickening made out; both knees can be completely extended; flexion beyond 135° in right and 100° in left, is painful and resisted by patient. *Feet* and *ankles,* negative. *Temperature,* 101°. *Urine,* negative. *Blood:* not examined.

Operation, April 29, 1904; Dr. Painter. Incisions made on both sides of patella of left knee about 10 cm. in length. The fibrous capsule was somewhat thickened, the synovial capsule much thickened and very villous. The villi were quite vascular, and in greatest abundance about the border of the patella and along the edge of the femoral condyles. There was no excess of fluid in the joint, but a blood-serum tube was inoculated with a loopful. The cartilage was clear and glistening, and not eroded. The ligamentum mucosum was considerably thickened. The villi here and about the condyles and patella were trimmed out and the capsule closed

with interrupted silk. Skin closed with continuous subcutaneous silkworm gut. A voluminous dry dressing was applied to the extended knee.

The skin sutures were removed at the end of one week, and moderate passive and active motion begun. On the twelfth day functional use was permitted. Operation on the other knee refused by patient.

May 14, 1904. Has been walking about for past two days with no pain or apparent weakness. General condition excellent. Discharged, with flannel bandage about knee, to report in one week.

The highest temperature was on admission, 101°, varying thereafter from normal to 99°.

Nothing has been heard from the patient since last note, and attempts to locate him have failed.

Bacteriological Report. A loopful of serum, obtained from the left knee-joint at operation, was inoculated into a tube of plain blood serum. Upon this, in pure culture, developed an organism whose morphological and cultural characteristics are described later in the outline. This tube was put on ice, and for lack of opportunity was not studied until five months later. It was feared the culture had died out through drying down of the medium, but being a spore-bearer it was readily revived in pure culture, and showed the same characteristics as before. Its identity is further established by the finding in the tissue removed at operation of an organism of the same morphology and staining (Gram's) properties, as well as by the results of animal experimentation.

The synovial tissue removed at operation was hardened in 80 per cent. alcohol for histological examination. It consisted of a large handful of coarse, thickly-set villi, not very vascular. Sections stained by the Gram-Weigert method showed the presence of the bacillus in small numbers, lying mainly in the lymph channels or cells at some distance from the free border. The character of the tissue corresponds histologically with the description in the introductory section. The animal experiments are described under a later heading.

Case II.—Aaron B. R., Nova Scotia; aged thirty-eight years; marine engineer. Admitted January 5, 1905. Carney Hospital, orthopedic service, Dr. Painter.

Complaint. Pain and swelling of right knee.

Family History. Negative; no joint affections.

Personal History. Has had various diseases of childhood. Gonorrhœa three times, the last fifteen years ago. No history of chronic diseases, nor of any previous joint troubles.

Present Illness. Seven months ago began to have sharp pains in right knee, radiating up the thigh, aggravated by frequent kneeling at work. One month ago joint was subjected to a sudden

strain; since then pain has been continuous, and joint swollen except for brief periods of enforced rest. Kept at work until a few weeks ago.

Physical Examination. Well developed and nourished, color good. Lungs, heart, and abdomen negative. Condition of glands not recorded. All joints negative except right knee. *Right knee:* Capsule much distended and patella floats. Thickened irregular masses can be felt, apparently within the capsule. Motions of joint considerably restricted. Circumference across patella 5.5 cm. greater than on left side; 3 cm. atrophy of right thigh and calf. *Temperature* normal. *Urine* negative. *Blood,* hæmoglobin, 80 per cent.; red blood corpuscles, 6,000,000; white blood corpuscles, 12,600.

Operation. January 10, 1905. Dr. Painter: Incision made on inner side of patella of right knee, about 8 cm. in length. Before opening the capsule all bleeding was controlled and wound well retracted. Through a small incision in the capsule about three ounces of serous fluid was allowed to escape into a sterile flask. Capsular incision was then extended. Bone and cartilage were normal. The whole synovial membrane was thickened and rough. Villous masses depended from the internal alar ligament, and a pannus-like fold of synovial membrane overlay the inner surface of the internal condyle. These tissues were removed, and operation completed as described in Case I., the after-treatment being carried out in same manner.

January 24th. Discharged, wearing flannel bandage over knee. Temperature practically normal throughout stay in hospital.

Bacteriological Report. 1. *Serum.* About ℥iij were obtained, rather syrupy and cloudy but not flakey, of light urinous color. 2 or 3 c.c. were removed with a sterile pipette, transferred to a tube of plain blood serum, and incubated at 37° C. No growth ever appeared on this tube, which was discarded after two weeks.

Two centrifuge tubes, which had previously been plugged with cotton and sterilized one and a half hours by dry heat at 150° C., were half-filled with serum removed with the sterile pipette, and contents centrifugalized for three minutes. From the bottom of one of these tubes two or three drops were removed with a freshly sterilized pipette, inoculated into a tube of plain blood serum, and incubated at 37° C. Smears were also made from the bottom of the centrifuge tube. These, like smears from the uncentrifugalized serum, showed only a quantity of fibrin and small numbers of red and white blood cells, probably blood flowing from nick in the capsule. The inoculated tube showed no visible growth after twenty-four hours; the surface of the serum was bathed with the water of condensation. Twenty-four hours later a plentiful growth of discrete, colorless, pinpoint colonies appeared in pure culture over the whole surface.

The remainder of the serum, about ℥iss, was transferred to a sterile Florence flask and incubated at 37° C. Four days later a drop from this flask showed presence in small numbers of an organism, morphologically the same as cultivated from centrifugalized portion, but clumped and immotile.

2. *Tissue.* This consisted of five or six small bits of rather lipomatous nature and not very vascular. The most vascular-looking bit was snipped several times with a pair of sterile scissors, quickly transferred with sterile forceps to a tube of plain blood serum, and incubated at 37° C. After twenty-four hours no growth was evident, and surface was bathed; after forty-eight hours it showed a growth identical with that from the centrifugalized serum, and examination showed presence of the same organism in pure culture. The cultural and morphological characteristics are later described in outline.

The remainder of the tissue was placed in 10 per cent. formalin for histological examination. Cut sections showed no peculiarities other than described in the introduction. The organism isolated does not stain by Gram's, but sections stained with polychrome methylene blue and eosin show the presence of the bacillus in very small numbers in the tissue.

Animal experiments are recorded later.

Case III.—Annie M. B., Massachusetts; aged forty years; single; music teacher. Admitted December 17, 1904. N. E. Baptist Hospital, Dr. Goldthwait.

Complaint. Pain and swelling in many joints, especially hands and elbows.

Family History. Mother died of cancer of stomach. Father died fourteen years ago of typhoid fever. Definite "rheumatic" history on the part of two maternal aunts, both being on crutches and crippled in many joints for ten years and twenty-five years, respectively.

Personal History. Measles and mumps in infancy. Typhoid fever fourteen years ago, at same time with father. No history of traumata or early joint troubles. Never robust, but always in fair health until attack of typhoid fever.

Present Illness. Began at age of twenty-six years, seven weeks after full convalescence from a typhoid fever unaccompanied by complications. An acute swelling developed suddenly in both wrists, coming and going irregularly. In the next few years various other joints became involved, especially of hands, elbows, knees, and feet, with occasional pain referred to hips. At various times the swellings have been very considerable, hot, red, and painful. They were never aspirated. Twelve years ago hands were so troublesome that work (stenography) was impossible. Much improved a year later, and for five years grew steadily better. An attack of influenza (?)

four years ago seemed not to affect joint conditions. Eighteen months ago had erysipelas of face, after which no trouble until a year later, when the frontal sinus was opened on account of a progressive swelling in left orbital region; character of pus not determined. Since that time, however, all joints have been worse, particularly in the hands, and the trouble has since appeared in the shoulders. The general health at present is fair, but the patient is in a nervous condition.

Physical Examination. Fairly well developed, poorly nourished, pale. *Heart* and *lungs* negative. *Abdomen* negative; spleen and liver not palpable. *Glands* slightly enlarged in neck and in both axillæ; epitrochlear glands not palpable.

Special Examination. Both sternoclavicular joints tender; slight swelling about both maxillary joints, and movements painful; spine apparently not involved. *Shoulders:* the right allows normal motion, but with much crepitation; the left shows same condition, but motions are all guarded. *Elbows:* both show normal amount of flexion, but stop short 20° of complete extension. *Wrists* and *hands:* distinct swelling of practically all the metacarpophalangeal and several interphalangeal articulations, with slight amount of ulnar deflection of both hands. Hips apparently not involved. *Knees:* motions somewhat guarded and painful in both joints; outlines practically normal. Both feet and ankles negative.

x-Ray: A good negative of both hands and wrists shows practically no alteration from normal in either bone or cartilage.

December 22, 1904. The two most swollen joints of the hands—the right middle metacarpophalangeal and the left middle proximal interphalangeal—were aspirated for bacteriological purposes.

23*d and* 25*th.* 6 c.c. and 8 c.c. of Aaronson's antistreptococcic serum injected into thigh muscles.

28*th.* Has been having evening temperature of 100° to 100.5°, with morning remissions to normal; pulse, 100; respirations, 24. To-day temperature rose to 101.4°; pulse, 120; respirations, 26. There was pain in right nipple line over liver. Transferred to Dr. Badger, account of pulmonary conditions.

30*th.* The picture is clinically of pneumonia, but examination is negative; some few friction rubs over base of right lung in front.

Leukocytes, 24,000. Urine negative. Respiration short, painful, shallow. No sputum.

January 1, 1905. Bronchial respiration over left base, behind.

3*d.* Pneumonia fully established in left lower lobe. Heart free.

6*th.* A to-and-fro pericardial rub without signs of fluid.

25*th.* Three ounces clear fluid withdrawn from pleural cavity. No culture made.

February 4*th.* Delayed resolution slowly clearing. Heart conditions have cleared. General condition much better. Joint symptoms have improved in a remarkable way.

March 11th. Lung is not wholly cleared; a little bronchial respiration still heard at left base, otherwise resonance and respiration good throughout. There has never been any sputum. The highest temperature was 103.2° on January 1st.

Discharged by Dr. Badger, well of pulmonary conditions* and with joints in better condition than for months.

Bacteriological Report. As noted above, one joint of each hand was aspirated under aseptic precautions, several days before onset of pulmonary symptoms. From each joint one small drop of serum was obtained, and from each one plain blood-serum tube was inoculated, and incubated at 37° C. Unfortunately no smears were made from the needle points. At the end of two weeks one tube was discarded, being sterile.

The tube inoculated from the right middle metacarpophalangeal joint showed no visible growth at end of twenty-four hours; surface was bathed with water of condensation. Twenty-four hours later a fine growth had appeared over surface of medium—colorless, glistening, pinpoint colonies in pure culture. Subcultures were made on various media. The organism is described in the outline later.

Animal inoculations are also recorded later.

The following case differs from the preceding three in being one of typical acute articular rheumatism.

CASE IV.—Solomon K., Russian Hebrew; aged nineteen years; papermaker. Admitted January 9, 1905. Carney Hospital, medical service, Dr. Minot.

Complaint. Knees painful.

Family History. Not obtained.

Personal History. "Rheumatism" twice before, last attack one year ago. Denies all acute infectious and venereal diseases.

Present Illness. Began December 14, 1904, with pain in ankles and left elbow. Three days later admitted to Boston City Hospital with temperature of 102.5°, pulse 120. Throat was found normal; no glandular enlargements. The left elbow was tender but not red; the right ankle and foot were tender, red, and swollen. Was given antirheumatic treatment, and being somewhat improved was discharged, January 5, 1905, to United States immigration authorities. January 9th admitted to Carney Hospital, saying he had caught cold the day before and could not walk because of pain in knees.

* Bannatyne,[7] speaking of the arthritic type to which this case belongs, says (p. 27): "I find that about 3 per cent. of my cases developed either pneumonia or pleurisy during the time they were under my care, and about 17 per cent. developed endocardial or pericardial conditions after the onset of the disease."

MORPHOLOGICAL AND CULTURAL CHARACTERISTICS.

	Bacillus No. 1. Case 1.	Bacillus No. 2. Case 2.	Bacillus No. 3. Case 3.	Bacillus No. 4. Case 4.
Morphology: shape	Long plump rods, with slightly rounded ends.	In first cultures diplococcoid, but after transplantation — plump rods of moderate length, with slightly rounded ends.	Pleomorphic.[2] Lanceolate diplococcoid forms; on favorable media single and diplobacilli, with rounded ends, generally lying in parallel clumps.	Long, plump rods, with slightly rounded ends.
arrangement	Single, in pairs or in long chains; no true branching forms found.	In pairs chiefly; also single forms and short chains; no true branching forms found.	.....	Single, in pairs, or in long chains; no true branching forms found.
size[1]	Width 0.5–0.68 μ; length 1–4.9 μ; averaging 1–2 μ.	Width 0.6 μ; length 1–2.4 μ.	Width 0.6–0.8 μ; length of elements 0.7–1 μ; length of pairs 1.08–2.36 μ.	Width 0.72–0.76 μ; length 1.6–4 μ; averaging 1.5–2.5 μ.
capsule	None demonstrated.	None demonstrated.	None demonstrated.	None demonstrated.
spores	Clostridium type; readily produced in old cultures.	Clostridium type; considerable numbers in 3-day blood-serum cultures.	None demonstrated.	Clostridium type; great numbers in 3-day bouillon cultures.
Motility	Actively motile.	Actively motile.	Non-motile.	Actively motile.
Staining properties	Stains readily with aniline dyes, and by Gram's.	Stains readily with aniline dyes, decolorized by Gram's; occasional polar granulation in old cultures.	Stains readily with aniline dyes, and by Gram's.	Stains readily with aniline dyes, decolorized by Gram's.
Cultural chars	Facultative anaërobe.	Facultative anaërobe.	Aërobic, practically no anaërobic growth.	Facultative anaërobe.
blood-serum, 37° C.	Grows vigorously, in 48 hours covering surface of medium and water of condensation with a thick, tough, corrugated pellicle of pale rose color; liquefaction of medium fairly rapid; not checked by icing.	Delicate growth as raised, viscid, colorless thin line; discrete colonies are round, raised, flat, colorless, pin-point, increasing to pin-head size in 2–3 days; no further increase.	Individual colonies same as of bacillus No. 2, but growth even less marked along streak, and not progressive.	Very vigorous growth, liquefaction beginning in 12 hours, and producing deep, viscid, yellowish furrows; a heavy, smooth, white pellicle rapidly covers water of condensation; discrete colonies minute, round, raised, moist, whitish, translucent, quickly fusing.
plain agar, 37° C.	Streak: grows well, in 24 hours showing a broad, elevated, white streak with moist, wrinkled surface, increasing but little after 48 hours, becoming powdery; individual colonies are minute, colorless dew-points, rapidly fusing. Stab: fair continuous growth, not increasing.	Streak: same as on blood serum at 24 hours, colonies later becoming ivory white. Stab: fair filamentous, continuous growth by third day, not increasing.	Streak: only a few smooth, round, flat, slightly elevated, discrete colonies, colorless, of pinpoint size, slowly increasing to diameter of 2 mm. and becoming whitish and crenated. Stab: very faint growth in depths.	Streak: after 24 hours, a slightly elevated, ivory white, broad streak, with irregular, smooth border; heavy, smooth, white pellicle over water of condensation; after 48 hours little change; no liquefaction. Stab: moderate, continuous, white growth after 24 hours, soon producing small, tuberous offshoots.

potato, 37° C.	At 24 hours a good growth; several large, viscid, white globules along an ill-defined, faint, pinkish streak, suggesting appearance of watermelon fibre; at 48 hours globules are collapsed, a wide-spread, rose colored growth in dew-point globules; later develops a blood-red color, not diffused.	Grows with difficulty, producing no visible changes.	Limited growth; moist, raised, whitish, almost invisible; typical forms in smears from scrapings.	At 24 hours raised, moist, sticky, lemon-colored growth of considerable vigor, in broad, irregular streak; medium slightly darkened; by fourth day growth has increased and become whitish, potato discolored brown; no further advance.
alkaline bouillon, 37° C.	Quickly becomes turbid; small waxy globules float on surface, later coalescing to form a firm pellicle, like honeycomb, over the whole surface.	Grows well, producing general turbidity in 24 hours.	Grows fairly well, producing slight general turbidity, and small amount of white, granular sediment.	Marked, rapid turbidity; by third day waxy scales float on surface, later uniting to form a dry, friable white pellicle.
litmus milk, 37° C.	Pellicle formed as on bouillon, finally firm enough to resist on inverting tube; slight alkaline reaction by fourth day, followed by bleaching: gradually acidified after 10 to 14 days; no definite clot.	Grows well, a faint alkaline reaction developing slowly.	Grows well, a faint alkaline reaction developing slowly.	A firmer pellicle than on bouillon; alkaline reaction on second day, followed by bleaching; turns acid in 7 to 10 days, with late formation of clot, digested slowly.
glucose gelatine, 20° C.	Stab: infundibuliform liquefaction, gradually reducing surface to level; fair growth in depth; no gas; pellicle faint rose in old cultures.	Stab: slowly produces slight, brown, granular growth in upper half, not advancing; no gas; no liquefaction.	Stab: barely perceptible whitish growth throughout stab, not progressing; no gas; no liquefaction.	Stab: infundibuliform liquefaction, gradually reducing surface to level; thick, sticky pellicle; no gas.
His' semisolid, 20° C.	No gas.	No gas.	No gas.	No gas.
Dunham's peptone, 37° C.	No indol.	No indol.	No indol.	No indol.
at 20° C.	Grows well on blood serum, but without pigment, and less vigorously than at 37° C.	Grows fairly well on blood serum, but soon dies out.	Grows weakly on blood serum.	On blood serum same as at 37° C., but more slowly.

[1] Fresh twenty-four-hour bouillon cultures stained with Loeffler's methylene blue.

[2] The unusual forms are described under section on "Animal Experimentation."

Physical Examination. Well developed and nourished. Pharynx congested. *Lungs* negative. *Heart* impulse diffuse over large part of præcordia; apex in fifth space, 11 cm. from midsternal line, not enlarged; sounds regular; blowing systolic murmur over whole præcordial area, loudest at apex, transmitted to axilla and back; second pulmonic sound accentuated; diastolic murmur, heard loudest at base in pulmonic area. *Abdomen* negative; liver and spleen not felt. *Knees*: Right shows but little swelling, not red or hot, moderately sensitive to pressure. Left somewhat swollen and warmer than right, but less sensitive. Both patellæ free, but motions are guarded. Aside from the knees the second phalangeal articulations of the middle fingers in both hands and the right wrist-joint were swollen.

Temperature on admission 100.5°. *Pulse*, 90. *Urine*, negative. *Blood:* Hæmoglobin, 90 per cent.; red blood corpuscles, 5,200,000; white blood corpuscles, 11,600.

The treatment is not of interest in this connection. By January 22d the joint conditions were considerably improved, but still complained of pain in elbow. The temperature, never higher than 100.5°, came down slowly. To escape the immigration officers the patient suddenly disappeared from view, January 29th.

Bacteriological Report. January 12th. Both knee-joints were aspirated under ethyl-chloride anæsthesia, after scrubbing with 80 per cent. alcohol. They had previously been prepared as described under the heading "Technique." From the right knee about two drops of serum were obtained and inoculated into a tube of plain blood serum; unfortunately not enough was left to inoculate a second tube. Smears were made from the needle point. The same description applies to the left knee. The smears were stained with gentian violet, and with Loeffler's methylene blue; a prolonged search revealed nothing but large mononuclear leukocytes in small numbers.

The tubes showed no visible change after incubation for eighteen hours; the surfaces of media were bathed with the water of condensation. Forty-eight hours after inoculation* pure cultures of the same organism had developed in both tubes, described subsequently in the outline.

Animal inoculations were carried out and are recorded in a later section.

CHARACTERS OF THE ORGANISMS FOUND IN THE FOUR POSITIVE CASES.

These are described in considerable completeness, not because the organisms themselves are of special interest, but for the better comparison with others they may resemble and with others found

* This forty-eight-hour incubation period does not suggest contamination; it was later observed in all cases in which organisms were recovered from joints of inoculated animals.

in cases of the same clinical types. It has not been possible to identify any of them with previously described organisms; in the attempt to do so reliance was placed chiefly in Chester's Manual.* (See tables pages 1066 and 1067).

ANIMAL EXPERIMENTATION.

Value of Evidence Afforded by Animal Experimentation. Three facts of importance here are to be deduced from the work done in this direction:

1. The well-established difference that various animals display, (*inter se* and compared with man), in their reactions to many organisms.

2. The greater resistance in general shown by animals as compared with man, more particularly in the case of organisms of slight pathogenicity.

3. The ability of a variety of *entirely distinct organisms* to produce in the joints of animals *changes indistinguishable clinically or pathologically.* This is well illustrated by the comparison of results obtained by Shaw[8] and by Cole,[9] in their milder cases, with those in my own series. Shaw worked with an organism from acute rheumatic joints. Cole employed virulent strains of streptococcus pyogenes.

From this it follows that:

1. The exact reproduction in animals of the lesions in human joints is, *a priori,* not to be expected.

2. Failure to produce *any* well-marked joint lesions is not to be interpreted as evidence of particular significance.

3. Positive results are no more than suggestive.

Report of Experiments.

In this work rabbits were inoculated, some intravenously and some directly into the joint. For the latter purpose the knee-joint was used; the left side was selected for experimentation, the right (with one exception, No. II., Case 1) was reserved for control. Both joints were shaved for comparison, and frequent observations were made both of local and general conditions. It may be said here that in no case did the general condition appear influenced by the treatment. Moreover, the animals inoculated intravenously never showed the slightest signs of articular disturbance, although large doses were administered in three cases, and in the fourth (No. IV., Case 1) 1.5 c.c. was injected, and the organism used had been passed several times through joints in which it excited an acute process.

* A Manual of Determinative Bacteriology, Macmillan Co., 1901.

Case 1. Rabbit I. Left knee.

October 5th. Received an initial dose of ɱviij bouillon suspension of a fresh blood-serum culture.* Only a transient inflammatory reaction followed, but after six weeks there gradually developed a periarticular thickening with signs of fluid in joint. At end of two months this condition was well established. Nine days after inoculation a pure culture was recovered by aspiration.

December 16th. Reinoculated with ɱij bouillon suspension from forty-eight-hour blood serum; the organism used was from a pure culture recovered from joint of Rabbit II. at autopsy.

The chronic condition became decidedly more marked, and joint was much distended with fluid; there was a persistent limp.

January 19th. Thirty-four days after last injection animal was chloroformed. *Left knee:* Capsule considerably distended and thickened; typical villous proliferation of synovial membrane; no acute inflammatory signs; bone apparently normal. Capsule contained about 2 c.c. of tenacious, whitish fluid containing a few flakes, which smears showed to be of nature of mild exudate; no organisms found in smears. Pure culture of original organism cultivated from joint fluid. The right knee appeared normal, as did all the internal organs. Joints were preserved as specimens.

Rabbit II. Both knees.

October 7th. Right knee inoculated with ɱviij from a pure blood-serum culture from joint of Rabbit I. (aspirated twenty-four hours after first injection).

10th. Left knee received ɱx suspension from recent blood serum culture. Four days later a pure culture was recovered and smears showed presence of a mild exudate, a few bacilli appearing in pairs. No clinical signs appeared in either joint.

27th. Died as result of an old process in lungs. Externally both joints appeared normal. The *right* showed only slight villous changes; smears and culture negative. The *left* contained an excess of fluid of exudative character, as shown in smears; there was distinct synovial thickening with congestion and, in places, typical villi. A pure culture was recovered from this joint. In paraffin sections from the synovial membrane histological changes were found, differing in no essential detail from those in the original human joint. Sections stained by the Gram-Weigert method showed the presence of organisms similarly situated in the tissues and identical in appearance with those found in the human villi. The liver showed small foci of coccidial disease. Both lungs contained large abscesses; the left was converted into a single large cavity containing about ℥ss of thin white pus. The nature of the latter process was not determined, but it clearly had nothing to do with the joint conditions and was evidently the cause of death.

* In the following notes, unless otherwise stated, it is to be understood that suspensions of twenty-four-hour blood serum were used for inoculations.

Rabbit III. Left knee.

October 12*th.* A pure culture from the joint of Rabbit II. was used; ɱviij were injected. A slight, transient, inflammatory reaction followed; a slight limp developed later.

December 16*th.* Reinoculated with ɱij from forty-eight-hour blood-serum subculture of organism isolated at autopsy from left knee of Rabbit II. Result slight.

24*th.* A final inoculation with ɱviij suspension from forty-eight-hour blood-serum culture, taken from joint of Rabbit I., resulted in a gradually increasing swelling, without acute signs, but causing limp. Eighteen days after inoculation a pure culture was recovered from the joint; smears showed existence of a considerable exudate.

The clinical signs had all disappeared at end of four weeks, but some capsular thickening persisted.

March 21*st.* Three months after last injection, chloroformed. *Left knee* showed merely a moderate degree of villous proliferation; smears and cultures negative. Joint saved as specimen. The right knee and internal organs appeared normal, and cultures from the heart blood, spleen, liver, and kidney were sterile.

Rabbit IV. Vein of ear.

January 18*th.* A twenty-four-hour bouillon subculture from joint of Rabbit III. was used; ɱxv were injected intravenously. No effects observed.

24*th.* 1.5 c.c. of a twenty-four-hour bouillon from same source injected. No effects whatever. Animal was still well until April 5th, when used for other purposes.

Case 2. Rabbit I. Vein of ear.

January 24*th.* 2 c.c. of twenty-four-hour bouillon culture, intravenously; no effects.

February 1*st.* Subcultures were made on blood serum from organism recovered from joint of Rabbit II. The growth on four twenty-four-hour blood-serum tubes was suspended in 5 c.c. of bouillon and injected into the vein. No effects. The animal is still well after eleven weeks.

Rabbit II. Left knee.

January 24*th.* ɱiv of twenty-four-hour bouillon caused only mild inflammatory signs, gone in forty-eight hours. The only time the organism was recovered from the joint was four days after this injection; it grew in pure culture; a very few organisms were also discovered in the smear from the joint fluid.

30*th.* Injected ɱiv suspension from forty-eight-hour blood-serum culture recovered from same joint. A slight reaction with moderate swelling, gone in two days.

February 16*th.* ɱv injected.

26*th.* ɱx injected.

In all, four inoculations were made but a satisfactory reaction was never obtained.

March 14*th*. Seven weeks after first inoculation, animal chloroformed. *Left knee* appeared practically normal, save for a few pale villi below the patella. Paraffin sections were made of these and the tissue was found lipomatous, in this respect resembling parts of the human tissue in this case. In one place a deposit of lime salts was found in the capsule. Staining with polychrome methylene blue and eosin failed to show presence of any organisms. There was no picture of acute infiltration, as in most of the sections from the human joint. Smears and cultures from this joint were negative. The right knee was normal, also the internal organs, cultures from which remained sterile.

Case 3. Guinea pig. Subcutaneous injection.

Of a twenty-four-hour bouillon culture $\frac{3}{4}$ c.c. was injected beneath skin over abdomen. Three weeks later a soft enlargement of glands in both groins appeared. No constitutional disturbance could be made out, and after three months animal was alive and well.

Rabbit A. Left knee.

January 19*th*. ɱiij of twenty-four-hour bouillon provoked little reaction.

28*th*. ɱvij from twenty-four-hour blood serum caused considerable swelling and some limp; practically normal by the fourth day.

February 8*th*. ɱx caused considerable swelling and some limp. Aspiration after five days showed presence of exudate and active phagocytosis in joint; culture sterile.

20*th*. Only a periarticular thickening remains. ɱiij injected. (Any effects of this inoculation were obscured by the development of an abscess located near, but outside the joint, having apparently nothing to do with the injections. Similar abscesses were present beneath the skin in other places before the injections were begun; the condition is very common in rabbits. The abscess in question disappeared in about ten days). A polar-staining bacillus, in pure culture, was obtained from the extra-articular abscess. As it was decolorized by Gram's it cannot be identified with the Gram-staining organism found later in sections from the synovial tissue.

March 2*d*. ɱx injected. No acute signs, but a considerable capsular distention and limp resulted, persisting until animal was killed.

The organisms were never recovered from the joint, though several attempts were made. As early as forty-eight hours after injection all organisms appeared to have been included by the phagocytes.

20*th*. Two months after first inoculation, animal chloroformed. The right knee and the internal organs appeared normal; cultures

from the latter remained sterile. *Left knee* contained about mvij of tenacious grayish exudate, from which cultures were sterile. Fibrous capsule normal, but there was a considerable uniform thickening of synovial capsule. A few minute villi hung by thread-like pedicles from the ligamentum mucosum; a few also projected from above the patella. These latter were sectioned in paraffin and stained by the Gram-Weigert method. Histologically, sections showed a moderate synovial thickening with presence, in considerable numbers, of the new tissue-forming cells; there was only a moderate degree of infiltration with small round cells and polymorphonuclears. Occasional sharply stained bacilli were found singly and in pairs. The latter were identical in size and appearance with certain forms occurring in the cultures from this case.

The following experiments were made with the view of identifying, if possible, these organisms with the ones injected—pleomorphism on artificial media having already been observed in the latter.

Rabbit IV., Case 1, was used, and on two different occasions 0.5 c.c. and 1 c.c. from twenty-four-hour cultures on blood serum were injected into the left knee-joint. Aspiration after twenty-four hours and eighteen hours, respectively, showed practically all the organisms included in phagocytes and incapable of staining by Gram's; cultures remained sterile. 25 c.c. of cloudy forty-eight-hour bouillon was then injected into the peritoneum, and after six hours a small quantity was withdrawn. In smears only a few organisms, and these of short forms, were found; many phagocytes appeared but the disappearance of the organisms seemed mainly due to bacteriolysis. Typical pure cultures grew in discrete colonies on blood serum.

Rabbit B. of this case was then similarly injected with 50 c.c. intraperitoneally. Two and three-quarter hours later a small quantity was withdrawn. Smears showed same picture as above, short pairs staining by Gram's being found free and in the leukocytes. Typical pure cultures grew in discrete colonies on blood serum.

After a few days both rabbits showed little sign of infection; it is too early to make any further report.

From the pure cultures in the last two cases smears were made on second and third days, and stained by Gram's. The majority of organisms were short diplobacilli; small coccus forms also occurred, and a small number of single long rods. The latter were measured with the micrometer and compared with the similarly stained organisms found in the tissue from Rabbit A. Here are the comparisons:

From cultures on blood serum: length in four cases: 1.9μ, 2.4μ, 3.1μ, 3.7μ.

From stained sections of synovial membrane: length in two cases: one diplobacillus, elements 1.3μ, pairs 2.8μ; one single rod, 3 (3.0μ). One or two longer forms in the tissues could not be measured, not lying in a horizontal plane.

Without cultures from the tissue the proof is incomplete, but the failure to obtain any growth from fluid aspirated on six different occasions speaks for the singleness of the infection.

Rabbit B. Vein of ear.

January 28*th.* A sterile water suspension of growth on four twenty-four-hour tubes of blood serum, intravenously, produced no noticeable effects. Ten weeks later this animal was used for intraperitoneal inoculation as noted above.

Case 4. Rabbit I. Left knee.

January 19*th.* ɳv of twenty-four-hour bouillon caused a fair inflammatory reaction with limp, lasting six days.

28*th.* ɳvij of twenty-four-hour bouillon caused less acute inflammatory change but more swelling and limp.

February 5*th.* ɳviij suspension of pure culture recovered from joint, and grown forty-eight hours on blood serum, produced a good local reaction with limp, and persistent swelling.

16*th.* ɳij as above from a recently recovered pure culture. No acute reaction.

28*th.* Swelling about gone. ɳxij caused a transient acute reaction, followed by a progressive swelling and limp, clearing after ten days.

March 18*th.* Eighteen days after last inoculation, animal chloroformed. The right knee and internal organs were normal. Cultures taken from the liver and spleen showed a few colonies of cocci, not pyogenic, and clearly not related to the experimental infection. *Left knee* contained slight serous exudate, from which the bacillus, in pure culture, was grown, and smears from which showed rare organisms, free and in the leukocytes. The synovial membrane was not congested, but bore patches of fine villi, a portion of which were taken for examination. A curious body, of the size, shape, and appearance of a small cantaloupe seed, lay in lower end of the lateral pouch outside the external condyle. It was attached by a long, thread-like pedicle to the inner side of the opposite condyle, where the synovial membrane had a fibrinous coating. Histologically, it was found to be organizing exudate. The villous specimen sectioned in paraffin, and stained with polychrome methylene blue and eosin, presented a beautiful histological picture, comparable to that in Case 1, but no organisms could be found after long search through many preparations.

Rabbit II. Vein of ear.

January 28*th.* 4 c.c. of twenty-four-hour bouillon.

February 6th. 3.5 c.c. suspension containing twenty-four-hour product of four tubes inoculated with pure culture from joint of Rabbit I.

After ten weeks no effects whatever have been detected.

III. Interpretation of Results.

This necessitates a consideration of the reports of other workers in this field. The findings in cases of acute articular rheumatism are not included here.

Bacteriological reports of other observers.

1. *Schüller.* This evidence is considered first, as it is the most extensive and applies without question to the described class of cases.

His first report[6] was in 1892, when he mentioned finding constantly, in cut sections of tissue from the joints, the same organisms described in later papers.

1893.[10] By tapping joints (with cannula, allowing serum to drop directly on media in tubes and plates) he obtained the same bacilli found previously in histological sections. They are described as *short, plump rods, showing polar granulation* distinct from spores; the latter appear, however, in old cultures. Rods measure 0.75μ to 0.99μ x 2.24μ to 2.76μ, and stain by ordinary methods, though easily decolorized; no note here or elsewhere of Gram's method. Grew well at 25° C. in dark. In gelatin stabs, small white granules along course of puncture, going on to liquefaction; plates show whitish-gray points. On agar, similar plaques; the same on potato. Cultures ten to twelve months old were revived and proved infectious. Inoculation into rabbits' joints of 0.5 to 1 gm. caused marked swelling of permanent character and persistent limp. Animals were killed at end of two months, prior to which original organisms were recovered from inoculated joints. Pus was never found in the experimental joints; synovial membrane bore, in places, pale and brownish villous fringes, sections of which were shown to contain the organism injected. The uninoculated joints displayed no changes. Subcutaneous injections caused no suppuration, only slight local induration, but doses of 0.5 to 1 gm., it is said, were fatal in twenty-four hours. Injection of like quantity into joint produced nothing like this fatal picture.

1896.[11] A quick method is described for demonstrating the organisms in human tissues. At operation, when the fringes protrude through the wound, they are washed off with sterile water or $HgCl_2$, split open with a fresh knife and a sterile glass slide drawn across the newly cut surface. Smear is air-dried and stained with carbol fuchsin.

1897.[8] In sixteen arthrotomies, in cases of the type differentiated, in smears from the freshly cut villi (after method described above), and later in sections from these tissues, the bacillus was constantly demonstrated, generally easily, as the organisms are actually in the tissues and much less frequently free in the joint fluid. In aspirating the needle should be thrust, he says, not into the joint cavity but into the synovial tissues, where the organisms actually are. Of twenty-three aspirations, six were negative. In the pathological tissues the organisms are found mostly at the site of the greatest changes. Cocci often appear together with the bacilli, both in aspirated material and that obtained at operation; in one aspiration cocci only were obtained. These appear identical with the pyogenic cocci and are not regarded as playing any important role, certainly not a causative one. A comparison is made with cases of joint tuberculosis, where the tubercle bacillus is often found in small numbers, while pyogenic cocci are abundant. The present bacillus is not easily demonstrated in sections, because so readily decolorized.

A later paper,[5] in 1900, adds nothing bacteriologically.

2. *Bannatyne,*[7] *Wohlmann and Blaxall,*[12] 1896. Next to Schüller's this is the most complete bacteriological report bearing on our subject. It is therefore necessary to examine carefully the nature of the cases from which the evidence is deduced.

It is clearly emphasized (p. 79[7]) that cases of the hypertrophic type of arthritis deformans are to be excluded, and that it is from certain acute polyarticular cases only that the organisms were isolated. These cases are defined in pp. 91 and 92, from which the following is quoted: "Dr. Still, in Clifford Allbutt's *Medicine*, says there is in children a disease which presents important differences both in its clinical symptoms and morbid anatomy, as well as one which is clinically analogous to the rheumatoid arthritis of adults. The first type of the disease is characterized by chronic progressive enlargement of the joints . . . the joint thickening affects the tissues round the joints, rather than the bones or cartilages. . . . The pure rheumatoid arthritis in children he considers to be characterized by bony thickening and lipping about the joints. . . . Now, his description of the first class corresponds with my description of what we see in adults in the acute form of the disease, and also his second with the chronic form."

It is from adult joints of the first type, acute at the onset but developing permanent changes not involving bone or cartilage, that the following bacteriological evidence was obtained. Further descriptions (pp. 93 and 94[7]) bear out the conviction that Bannatyne is here dealing, in part at least, with the *polyarthritis chronica villosa* of Schüller, with whose work, and that of Chauffard and Ramond,[13] he compares his own bacteriological results.

To turn to these now, as summed up in the conclusion of Blaxall's report:[12]

"1. In the synovial fluid in eighteen cases of rheumatoid arthritis an organism has been demonstrated, which is constant in its characteristics.

"2. The organism is a minute bacillus, exhibiting marked polar staining. It is difficult to stain and easily decolorized.

"3. The organism can be grown in culture media, and presents striking characteristics. In beef-broth it gives the appearance of gold dust; and on agar-agar and serum its growth is almost invisible.

"It does not grow on nutrient gelatin at ordinary temperature.

"4. It is present in the blood of severe cases.

"5. It has not been found in the synovial fluid from distended joints due to other causes."

Two years later Bannatyne[7] states that in the few sections he was able to obtain, the same bacillus was found in the cartilages, synovial membrane, and periarticular tissues.

A special method for cultivation and an elaborate technique for staining were employed. The organism is described as averaging 0.6μ x 2μ, not occurring in chains, non-mobile, decolorized by Gram's, and in general requiring special care in staining. For further accounts of cultural characteristics, etc., reference should be made to Blaxall's report.[12]

Inoculations of mice, guinea-pigs, and rabbits were without results.

The bacillus is differentiated from Schüller's. It is mentioned in comparison with that found by Chauffard and Ramond, which, it is incorrectly stated (p. 83[7]), they "cultivated" from the synovial fluid.

Though a firm believer in the infectious origin of these cases, Bannatyne is uncertain as to the role played by the organism he has found.

3. *Von Dungern and Schneider*,[14] 1898. This is an account of a single case, very like, except for its fatal result, to my Case 1.

Man, aged forty-four years; acute polyarticular attack, subsiding after five months, leaving heart lesion; complete freedom for twelve years, when a second attack left him with permanent joint changes and some spinal rigidity; these conditions were still present five years later, when death occurred from inanition. At autopsy, characteristic changes were found in the joint synovial membranes, but with thinning of cartilage.*

The bacteriological report is of interest. It is based on a study of: 1. Aspirated fluid from finger-joints and blood from vein of arm (taken six months before death). 2. (Taken eighteen hours after

* On the basis of this latter fact the authors thought to distinguish this case from the type described by Schüller. It has already been pointed out, however, that such changes are not uncommon as secondary to long disuse or unusual severity of the local process, both of which features were present in this case; the patient had been completely bedridden for seven months before death.

death), fluid from several joints, heart blood, spleen, liver, kidneys, mucus from gall-bladder. Nothing was obtained from blood, spleen, or kidneys.

In smears a small diplococcus was found from the gall-bladder and cultivated on various media. The same organism was cultivated from the joint fluid and the liver. Morphologically, it much resembled diplococcus lanceolatus, grew in pairs, singly, or in chains up to ten, the pairs being 0.6μ wide x 1 to 2μ long, involution forms occurring. On agar small, discrete, transparent colonies were produced; on potatoes a white, granular growth, not elevated; on glucose agar after twenty-four hours a heavy confluent growth; milk acidified and coagulated in twenty-four to forty-eight hours; viability on artificial media demonstrated for at least three months. It was not identified with any previously described organisms. The joint lesions were reproduced by intra-articular inoculation in rabbits; importance was attached to the destructive changes* produced in the cartilages (not caused by Schüller's organism nor by control injections of pyogenic and other cocci, although villous and purulent conditions resulted from the latter). The diplococci were recovered and cultivated four to six weeks after injection.

From the liver and gall-bladder of this case, beside the diplococci, one other organism was found, from its morphology, cultural characteristics, and pathogenicity for animals, probably bacillus coli. From the joint fluid taken intra vitam a non-pathogenic coccus also grew; from that obtained postmortem there occurred, together with the diplococcus, a non-pathogenic bacillus.

The following conclusions were reached:

Not much importance is attached to these other organisms, yet it cannot be proven that the last two did not take part in the joint processes. Lesions once produced in joints render the latter favorable seats of infection. A good illustration is our finding there organisms of ordinarily such slight pathogenicity. It is possible that the diplococcus infection itself was not established by one invasion, but by successive attacks, these organisms being particularly abundant in the chronically diseased gall-bladder.

4. *Chauffard and Ramond*,[13] 1896. In a communication entitled "Des Adénopathies dans le Rheumatisme Chronique Infectieux" descriptions are given of seven cases. Excepting two that are probably of gonorrhœal origin these are evidently of Schüller's type. In all cases the anatomically related glands were distinctly enlarged; in two, valvular heart lesions existed. The bacteriological evidence is admittedly slender, and was sought in but one case. The joint fluid was twice aspirated and inoculated directly into tubes and animals, with negative results. The two

* The little reliance to be placed in inferences drawn from lesions produced in animal joints has already been referred to.

epitrochlear glands were extirpated with strict asepsis. Of each a part was triturated and inoculated into culture tubes and various animals, with negative results; in histological examination of the remaining parts no organisms were found. Smears previously made from cut surfaces of the glands, and from the joint fluid, showed apparently the same organisms—short, fine diplobacilli, staining with the ordinary dyes, and not decolorized by Gram's.

Because of the frequent reference made to it by various authors, this report has been detailed to show its admitted lack of bacteriological value. It will not be referred to again.

5. *Bouchard and Charrin*,[15] 1891, 1894. These reports are also frequently referred to. The finding of pyogenic cocci in twenty-two cases of chronic joints is related, but the bare statements to this effect carry with them no conviction and do not require our consideration.

DEDUCTIONS.

It is not justifiable to base an opinion as to the etiology of a large group of cases, however much they may resemble each other clinically, upon a study of so few of its members. So much incredulity has been shown by the profession in general, with regard to the bacteriological reports previously made in rheumatic cases of various types, that pains have been taken in this paper to go into much detail.

Infectious Polyarthritis Chronica Villosa.

Case 1. The chain of evidence, so far as it is to be considered as such, is complete. The organism was isolated in pure culture from one of several joints in which the process had been recently active, and clinically typical. Histologically, it was found alone in the synovial tissue, included in the cells in an evident causal relationship. It was cultivated on artificial media. Injected into the joints of rabbits, it there provoked both acute and chronic processes, in nowise differing clinically or pathologically from those in the human joint. The organism was isolated repeatedly in pure culture from the animal joints, and sections from the tissues of the latter showed the presence in small numbers of this organism alone, similarly situated to those in the human tissue. Subcutaneously and intravenously moderate doses of exalted virulence were without effect.

Case 2. The organism in this case was isolated in pure culture, both from the synovial fluid and from the tissue, and grown artificially. Its presence was demonstrated in the human tissue, as in the preceding case. Though recovered in pure culture from the animal joint into which it had been inoculated, it failed there to produce any marked changes. Large doses intravenously were without effect.

Case 3. From one of two joints which were aspirated an organism was obtained in pure culture, under conditions that left little doubt that it played some role in the morbid process. Animal experimentation produced the same satisfactory results as in Case 1. Large doses intravenously proved harmless.

From each of these three cases a single different organism was isolated, apparently capable of considerable resistance under artificial conditions.

The findings in these cases differ from those of Schüller, who found in his own cases the same organism constantly. Bannatyne likewise, in the same type of cases, constantly found a single organism, but it was not Schüller's. It is impossible to explain the constancy of Schüller's results or of Bannatyne's. It is clear that they worked with the same type of cases as my own.

From the reports of previous observers, then, we should be inclined to believe that these cases are undoubtedly of bacterial origin, but that a variety of organisms may be responsible for the mischief. My observations serve to confirm this belief.

Nevertheless, even with a chain of evidence as complete as furnished in my Case 1, the possibility must not be overlooked that we may have been dealing throughout with organisms which invaded the joints only after the working of some other process had rendered them liable to infection. There can be no doubt that this may occur. In Case 2 the traumatic factor seems to have determined the unusual localization in a single joint; it is conceivable that in the absence of this factor the organism found there would have come to an untimely end without producing any more effects than in the healthy rabbit into which it was inoculated.

But the evident infectious character of the onset and of the whole clinical picture in these cases is suggestive. In the same way that predisposition toward all disease in general is determined, the local infectious process appears to be secondary to some factor which lowers the general or local resistance, rather than to any other preceding involvement of the joint—in other words, the joint disturbances are doubtless, *ab initio*, simple infections, but like all conditions of this nature, are much more frequent in individuals whose general condition is below par. As to the constitutional disturbances that frequently mark the onset, we may conceive of them in two ways—as manifestations of a general infection that soon becomes localized in the joints, or, as seems less likely, as caused by secondary general intoxication or actual infection succeeding an initial joint infection.

As to the probable *portals of entry* of such organisms, the same considerations apply here as in the case of a great variety of ordinarily saprophytic or weakly pathogenic organisms, which, under favorable circumstances, are capable of provoking local or even general disturbance. It is not within the province of this report

to deal with this phase of the subject. I would merely refer, in passing, to the important work of Adami[16] in this direction, and its abundant confirmation by subsequent observers. A recent communication by Wrzosek[17] promises to shed new light on this matter.

Acute Articular Rheumatism.

Case 4. In this case the same organism was isolated in pure culture from each knee by aspiration. It was artificially cultivated and reproduced satisfactory lesions, clinically and pathologically, in the animal joint into which it was inoculated. It was several times isolated from the latter in pure culture, but could not be demonstrated in the lesions.

With regard to the causal relationship of this organism to the local joint disturbances, the same conclusions apply as in Case 3. The actual heart lesions in acute articular rheumatism, apart from the joints, are too various to consider here.

Relationship of Acute Articular Rheumatism with Infectious Polyarthritis Chronica Villosa.

To the great number of observations recorded in the bacteriological study of acute articular rheumatism I can only refer in general. The results are more at variance than in the less investigated field of infectious polyarthritis chronica villosa. The sum total of evidence, however, is in favor of a varied bacterial origin. Even the emphatic claims of recent English observers to have found a specific cause in the so-called "micrococcus rheumaticus" have been well answered.[9]

Clinically and pathologically, as I have been at pains to point out, the class of cases described by Schüller are distinct from acute articular rheumatism.

Commonly coming under observation only after the chronic condition has developed, their infectious nature is often not recognized, nor is the futility of commonly applied methods of treatment—(dietary, hydrotherapeutic, massage, etc.)—appreciated. The frequent indications for operative interference* explain the interest of these cases to the orthopedic surgeon.

Bacteriologically, however, there is no evidence to show that there is any essential difference between acute articular rheumatism and infectious polyarthritis chronica villosa. The difference in the subsequent course of the two conditions is apparently due to differences in the infecting organisms and in the degree of disturbance they are capable of provoking.

This conception of a similar though not identical etiological

* It is to be noted that in resorting to surgical measures care must be taken to exclude *atrophic arthritis*, as such treatment is to be applied to this type only in selected cases.

relationship is no indication, as I have said, that the two types should not be sharply separated clinically. That this differentiation cannot always be complete must be very evident; points of resemblance occur when, in the chronic type, the general disturbance is considerable and the heart is affected, as in Case 1.

The necessity of a similar bacteriological study of a large number of cases is clear.

It is surprising that with the great interest in bacteriological research in this country, we should have failed to recognize the significance of Schüller's and of Bannatyne's work, and that we have contributed so little to the investigation of this large and important group of cases. No satisfactory work has been done in the bacteriological examination of blood in these cases. This should be a field of special interest, for it is to be pointed out that practically all the results reported in bacteriological study of acute articular rheumatism proceeded from the investigation of materials* other than the joint fluid.

To Dr. Timothy Leary, of Tufts College Medical School, in whose laboratory this work was carried out, I am grateful for much assistance and friendly courtesy. The kindness of Dr. Charles F. Painter, in providing me with the clinical material, is gladly acknowledged. My thanks are due also to Dr. J. E. Goldthwait, to Dr. J. J. Minot, and to Dr. George Badger for clinical notes and materials.

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* From a fairly complete list of the most important bacteriological work in acute articular rheumatism I have made out a table showing the character of the findings. Out of the positive results of 91 examinations from different materials, 18 were from the blood, 9 from joint fluid, and the rest from various other sources (autopsy materials, excised tonsils, urine, etc.). This does not show the proportion of cases in which the joint fluid was examined without results; there it would appear very much smaller.

A FATAL CASE OF STOKES-ADAMS DISEASE WITH AUTOPSY, SHOWING INVOLVEMENT OF THE AURICULOVENTRICULAR BUNDLE OF HIS.

A PRELIMINARY COMMUNICATION.

By Alfred Stengel, M.D.,
PROFESSOR OF CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

The symptom-group known as Stokes-Adams' disease was first recognized by Adams in 1827, but more accurately described by Stokes in 1846. In recent years the subject has been discussed by Huchard in France, His, Hoffmann, and Jacquet in Germany, and by Prentis, Edes, Osler, and Babcock in America.

The symptoms that characterize the affection are: 1. *Slow pulse*, the rate falling temporarily or permanently to 30, 20, or even less. 2. *Cerebral attacks*, such as vertigo, syncopal or epileptiform seizures, unconsciousness. 3. *Pulsation of the veins in the neck* exceeding in rate the pulsation of the arteries twofold, threefold, fourfold or more. The disease was first recognized in old persons and in such as presented clinical or postmortem evidences of cardiac and vascular disease. Later instances were met with in younger persons and in some cases no lesion of any sort was found at autopsy. In Edes' series reference was made to the condition of the heart and vessels in 31 of the 35 cases that came to autopsy. In 26 of these sclerotic and myocardial changes were observed. In some cases lesions of the nervous system, such as compression of the medulla or changes in the vagus and cardiac plexus, have been described.

Recently, the resemblance of the clinical symptoms to the phenomena of "*heart block*," as produced by physiologists, has been pointed out. Gaskell first showed that constriction of the circular layer of muscle at the auriculoventricular junction of the heart of tortoises causes a cessation of the rhythmic action of the heart so that the auricles and ventricles become independent in their contractions, the former beating more rapidly than the latter. Various physiologists have confirmed this discovery and have discussed the nature of the mechanism which controls the rhythmic contractions. The prevailing opinion of physiologists at the present time is that the impulse to contraction originates at the large venous openings into the auricles and is propagated downward through the auricle into the ventricle within the muscle tissue itself. In a review of the evidence bearing on the transmission through the

muscle of the impulse to contraction, His[1] states that there are grave difficulties in the way of those who believe that nerve centres are the basis of cardiac activity. Rhythmic contractions certainly occur in the severed apex of a frog's heart after the contractions have been set in motion by some excitation. "Automatism," or *power of automatic contraction*, is therefore wanting, but there is present a *capacity for rhythmic contractility* after a stimulus has been given. Automatism in the frog's heart is found only in parts adjoining the auriculoventricular zone and the sinus region where there are ganglion cells. It does, however, also exist in embryonal hearts before ganglion cells are developed, though the experiments of Fano showed that even in such embryonal hearts the automatism is greatest near the sinuses and decreases progressively toward the apex of the ventricle. Physiologists agree that the ganglion cells at the venous sinuses are the principal source of the impulses for cardiac contraction, but Gaskell and Wooldridge proved that the nervous connections between auricles and ventricles may be severed without cessation of the ventricular contraction, and Krehl and Romberg have shown that in the adult heart the ganglia may be wholly separated without influencing cardiac contraction. The effect of the operation in the experiments of the latter authors was so slight that the heart maintained a blood pressure of practically normal degree. It would seem, therefore, that the impulse for contraction is transmitted from the sinus region to the auricle and ventricle through the muscle cells rather than through any nervous path. As a further evidence suggestive of this view Gaskell found that by stimulating the aortic bulb contractions could be made to run from ventricle to auricle; that is, in a direction the reverse of the normal. These experiments His regards as strongly antagonistic to the assumption that the impulse flows through a nervous mechanism.

If then the impulse travels through the muscle cells, it is necessary that a muscular connection be shown to exist between auricle and ventricle. Wm. His, Jr., first accurately described this connection in the mammalian heart in the form of a bundle of muscular tissue extending from the right side of the interauricular septum to the interventricular septum immediately below the *pars membranacea*. The "auriculoventricular bundle of His" is approximately 18 mm. long, 2.5 mm. broad, 1.5 mm. thick (Retzer). His' observation has been confirmed by Retzer, Bräunig, Humblet, and others. Though this bundle is an insignificant structure, physiological and anatomical evidence points to it as the pathway of the stimulus to contraction. In his experiments with Graufner, His found that by introducing a delicate knife through the auricle and dividing

[1] Wien. med. Blätter, November, 1894.

the auriculoventricular bundle in the septum (in rabbits) the auricles and ventricles ceased beating at the same rate. When the experiment was accurately performed the resulting condition was that of complete heart block, the auricles and ventricles beating independently of each other. A similar result has been obtained by Tigerstedt, who succeeded with a special appliance in compressing the auriculoventricular connections without hemorrhage and in producing the condition of heart block.

The most convincing experiments in this direction are those of Erlanger, who operated on the intact heart of dogs and other animals. With the aid of a specially devised curved needle, acting as a clamp, he was able to reach the auriculoventricular bundle of His by introducing the needle behind the posterior aortic leaflet and pushing the point through the interventricular septum. When the clamp was adjusted it was found that the muscle bundle of His alone was involved in the compression if the experiment was accurately performed. The amount of pressure could be regulated by means of a thumb-screw and complete or partial constriction could thus be established. The result of such compression was to produce first occasional failure of ventricular contraction; next, a ratio of the auricular to the ventricular beats of 2 to 1, 3 to 1, 4 to 1, and finally complete heart block in which the ventricles contracted independently of the auricular rhythm. Sometimes at the moment when complete block was established the ventricle ceased beating for periods varying from a few seconds up to fifty-five seconds. This phenomenon Erlanger explains as probably resulting from the fact that a certain time is necessary after complete severance of the connection between auricles and ventricles for the development in the ventricle of its inherent rhythmicity.

The experiments of Gaskell, His, Tigerstedt, Erlanger and others practically establish the fact that experimental heart block and the phenomena of Stokes-Adams' disease are identical. Up to the present communication, however, no case has been observed pathologically in which a lesion has been found involving the bundle of His. Dr. Erlanger tells me that when presenting his experimental work he suggested the possibility of involvement of His' bundle by a patch of sclerotic endocarditis beginning on the anterior mitral leaflet at its base and aortic border and extending to the interventricular septum where the bundle of His passes upward toward the auricle. The case about to be reported confirms the accuracy of his prediction.

J. B., aged fifty-seven years, a native of Germany, a wheelwright, was referred to the Out-patient Department of the University Hospital by Dr. B. F. Wentz, and to the medical ward by Dr. H. D. Jump. The patient was a married man, the father of five children, two of whom died in infancy: one of pneumonia, the other

of measles. He had been a healthy man, the only illnesses remembered by him being slight attacks of influenza, malaria, and lumbago. He denied venereal history, and there was no evidence of any such infection. He had never had any severe injury to the head or other parts of the body. He used tobacco in moderation, but had drunk beer to excess until two years ago, after which time he was very moderate in its use. The fatal illness began without warning while at his work about two and a half years ago. He suddenly fell backward and became unconscious for a few moments. There were no convulsive movements and he did not bite his tongue. The bladder was not emptied. He very speedily recovered from this attack and went back to work. Three months later he had another exactly similar attack and then the attacks came on in more rapid succession, about every two or three weeks. Except in the first attack he said he always fell forward. Two years ago he sometimes had spasmodic movements in the legs during the attacks, but the seizures were of varying severity, sometimes being extremely mild, when the patient did not fall nor lose consciousness but merely became slightly giddy for a few moments. In such mild attacks he was able by holding to some object to steady himself and prevent his falling. He found that stooping was more likely to provoke the attacks than any other movement or exercise. He has been troubled with flatulence after eating and has had obstinate constipation. Sometimes the attacks came on while eating, and occasionally belching would prevent their occurrence. At times there was pain in the head before the attack was fully developed and less severe headache was almost constantly present. He noticed that his face became cyanosed before the attacks and his friends observed that the cyanosis was intense during the attacks. After the seizure there was always violent palpitation.

The patient stopped working in May, 1905, and went to bed. During June there was a series of attacks, one following another every few minutes. Later they were less frequent, but he continued to suffer with the attacks until his admission to the hospital. He has lost sixty pounds in weight and has grown steadily weaker. He never had œdema nor dyspnœa.

Condition on Admission. The patient was admitted to the University Hospital on September 19, 1905, when the following notes were recorded:

The patient is a fairly well-nourished man; no cyanosis nor jaundice. There is marked pulsation in the epigastrium and in the veins of the neck. There is also visible pulsation of the brachial arteries. Radial pulses equal and synchronous; rate 36 and the character of the pulse "slow" (pulsus tardus). The radial and brachial arteries are somewhat hard. The pulse tension is moderately increased.

No enlargement of superficial lymphatic glands.

Eyes, nose, mouth, and ears normal; tongue slightly coated; teeth in fair condition.

Chest somewhat increased in the anteroposterior diameter; intercostal angle wide. Moderate depressions above and below the clavicles. Decided pulsation in the supraclavicular fossæ. Chest expansion fair and equal on both sides.

Apex beat visible in the fifth space just outside the midclavicular line. The impulse is moderately strong and there is a systolic thrill accompanying the beat.

Vocal fremitus is slightly diminished over the entire chest.

Percussion. The pulmonary note is everywhere slightly hyperresonant. Heart outlines: from the third space above to the sixth rib below and from the midsternum on the right to a point just outside the midclavicular line on the left.

Auscultation. The breath sounds are moderately weak, the expiratory sound slightly prolonged. There are no rales.

A somewhat harsh systolic murmur is heard at the apex of the heart and transmitted to the axilla. It is also heard toward the base of the heart. The second pulmonary sound is not accentuated, but is hollow and distant in character.

Abdomen. Epigastric pulsation is marked. Liver dulness begins at the sixth space and extends to the costal margin. Splenic dulness is normal in extent and the spleen cannot be felt.

The extremities are normal in appearance; reflexes normal. Station, gait, and muscular co-ordination normal.

Examination of the Urine. Specific gravity 1018, straw color, clear; reaction acid; no albumin; no sugar. Microscopically, a few hyaline and granular casts and scattered leukocytes were found.

September 22, 1905. The patient's condition has remained the same as on admission. There have not been any attacks and he feels quite comfortable.

Blood Examination. Red blood corpuscles, 5,260,000; white blood corpuscles, 14,000; hæmoglobin, 85 per cent.

23*d*. The patient began to have attacks this morning, a number occurring during the day. They have been mild in character, beginning with a momentary pallor, then a flushing or cyanosis and slight tremor of the arms. After the attack the face is pale and gradually the color returns. During several of the attacks it was noticed that the pulse stopped beating for a few seconds, and during one attack the interval was fifteen seconds. After the attack the pulse rate increased for a short time, then subsided to a steady rate of from 16 to 18 per minute. The pulsation of the veins in the neck continued during as well as between the attacks at from 80 to 100.

No change has occurred in the physical signs since the attacks have begun.

24*th*. The attacks are continuing at about one-half hour intervals. The pulse during the day has been from 18 to 26 and the volume has been good. The character of the attacks has not changed. During the seizures there seems to be only partial unconsciousness lasting a few seconds. The tremor attending the attacks is very slight. The eyes sometimes roll or move rapidly from side to side or upward in the earlier part of the attack and become fixed in a staring position when the attacks subside. The patient is quite weak and very nervous.

25*th*. The patient's strength has improved, as the attacks have been much less frequent.

26*th*. The paroxysms have grown more frequent and more marked. The development of the seizures to-day has been in the following order: The face first becomes yellow or pallid and the lips cyanosed; the eyes become fixed and staring, then move upward and to the left; the pupils change from a moderately contracted to a somewhat dilated condition, then the arms become a little rigid and tremble. The legs move very slightly in the same fashion. The pulsation at the wrist stops a few minutes before or during the attacks, and during one of the seizures the interval was thirty seconds. The venous pulsations in the neck continue through the attack. After the paroxysm the face becomes moderately flushed; the pulse begins to beat strongly, the respirations become deeper and more rapid than during the attacks. Unconsciousness is to-day somewhat more complete and of longer duration than previously.

During the afternoon the patient began to vomit, the first vomiting occurring just before an attack. Before and during the beginning of every seizure in the afternoon the pulse at the wrist stopped for from fifteen to twenty-five seconds.

27*th*. The patient is weaker and is becoming slightly drowsy. He slept poorly during the night and vomited repeatedly. After midnight the attacks followed each other in rapid succession. The seizures this morning are very severe. During one the pulse stopped for *two minutes and ten seconds*. The convulsive movements always follow the cessation of the radial pulse, and it is noticed that the face always becomes flushed before the patient recovers consciousness. The following table shows the duration of the cessation of the radial pulse, the number of venous pulsations in the neck per minute, and the rate of the radial pulse immediately after the attacks and some time later:

10.22 A. M. Ventricular beat for five minutes between attacks 147 per minute.

	Cessation of pulse.	*Venous pulse in neck.*	*Radial pulse.*
10.27	45 sec.	144	122
			1 min. later 24
11.20	80 sec.	140	132
			30 sec. later 84
			1 min. later 50
			2 " " 22
12.03	50 sec.	118	100
			1 min. later 80
			1½ " " 24
12.10	2 min. 10 sec.	120	90
			1 min. later 40
			1½ " " 38
12.20	Several attacks in rapid succession.		
1.00 P. M.	50 sec.	.....	96
			1½ min. later 20
1.30	1 min. 20 sec.	.....	100
			1 min. later 40

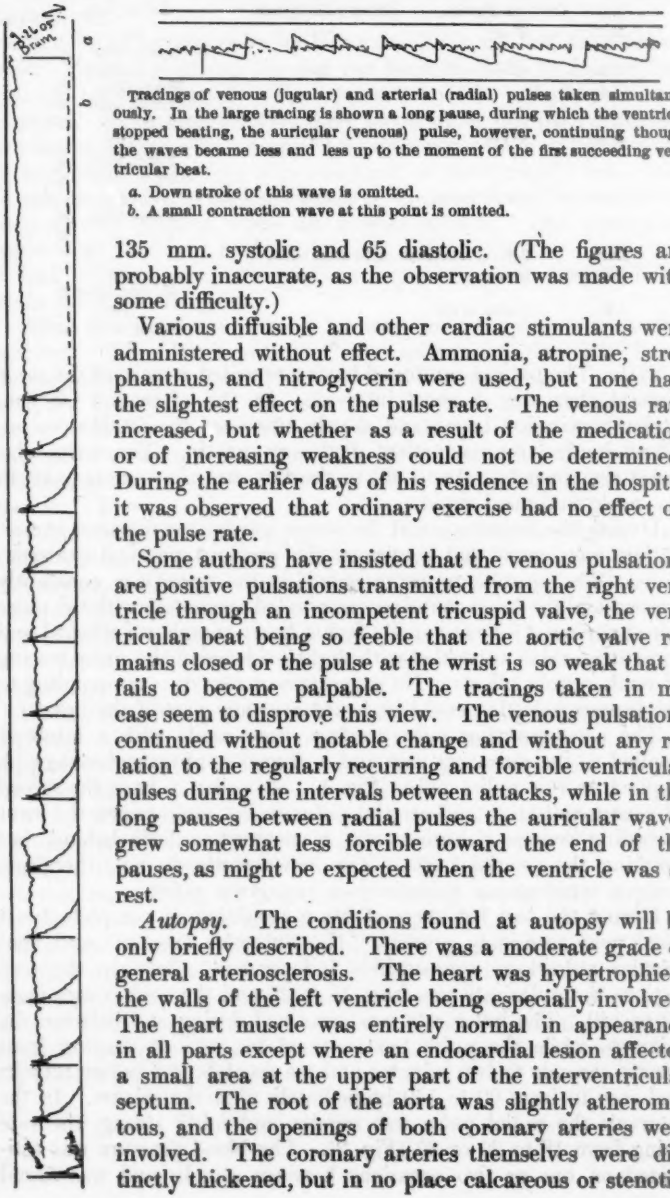
27*th*. The patient continued having repeated attacks of the same general character at short intervals. In the afternoon Cheyne-Stokes respiration began and shortly afterward the attacks ceased. Three hours later the patient died very quietly. The ventricular pulse remained low (18 to 26) to the last and the venous pulse in the neck continued rapid.

During the continuance of the severe paroxysms repeated examinations were made and confirmed the previous physical examinations. The systolic murmur heard at the apex was constantly present and the heart sounds corresponded accurately with the pulse felt at the wrist. Occasionally feeble heart sounds were heard and sometimes these coincided with slight evidence in the pulse tracing of weak systolic efforts. No suggestion of sounds corresponding to the venous pulsation could be heard over any part of the heart.

The accompanying pulse tracings were made with a tambour applied to the pulsating vein and a Jaquet's sphygmochronograph applied to the radial pulse (Fig. 1). In order to have the record of venous pulsation and arterial pulse on the same paper, the lever recording venous pulsations was of necessity a little behind that marking the arterial beats. The two records do not, therefore, present synchronous pulsations at any given point.

During the last few days of life a condition of complete heart block was seemingly present. The auricular (venous) and ventricular pulsations were entirely independent. Between the paroxysms the pulse rate was from 18 to 26 and the venous rate from 80 to 140. The latter rate was sustained during and between the seizures, while the pulse beats ceased for periods varying from twenty seconds to two minutes and ten seconds just before attacks and rose to from 90 to 140 immediately after the seizure. In the intervals the radial pulse was regular and fairly strong, the rate being from 18 to 20 or 30 (Fig. 2). The blood pressure was estimated on one or two occasions between attacks and was found

FIG. 1



Tracings of venous (jugular) and arterial (radial) pulses taken simultaneously. In the large tracing is shown a long pause, during which the ventricle stopped beating, the auricular (venous) pulse, however, continuing though the waves became less and less up to the moment of the first succeeding ventricular beat.

a. Down stroke of this wave is omitted.

b. A small contraction wave at this point is omitted.

135 mm. systolic and 65 diastolic. (The figures are probably inaccurate, as the observation was made with some difficulty.)

Various diffusible and other cardiac stimulants were administered without effect. Ammonia, atropine, strophanthus, and nitroglycerin were used, but none had the slightest effect on the pulse rate. The venous rate increased, but whether as a result of the medication or of increasing weakness could not be determined. During the earlier days of his residence in the hospital it was observed that ordinary exercise had no effect on the pulse rate.

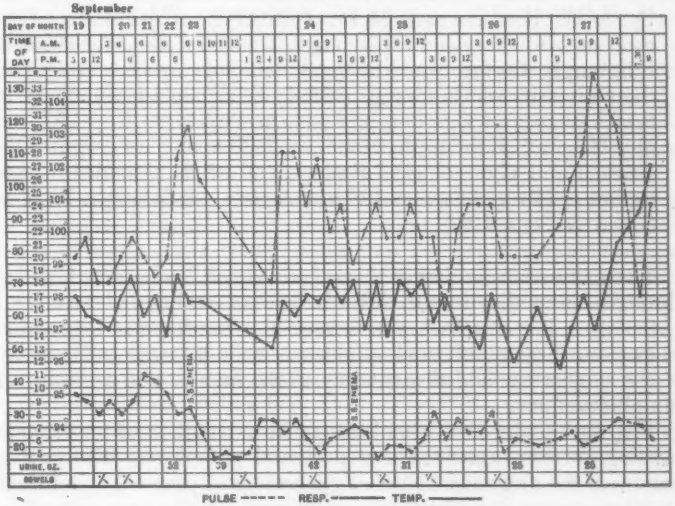
Some authors have insisted that the venous pulsations are positive pulsations transmitted from the right ventricle through an incompetent tricuspid valve, the ventricular beat being so feeble that the aortic valve remains closed or the pulse at the wrist is so weak that it fails to become palpable. The tracings taken in my case seem to disprove this view. The venous pulsations continued without notable change and without any relation to the regularly recurring and forcible ventricular pulses during the intervals between attacks, while in the long pauses between radial pulses the auricular waves grew somewhat less forcible toward the end of the pauses, as might be expected when the ventricle was at rest.

Autopsy. The conditions found at autopsy will be only briefly described. There was a moderate grade of general arteriosclerosis. The heart was hypertrophied, the walls of the left ventricle being especially involved. The heart muscle was entirely normal in appearance in all parts except where an endocardial lesion affected a small area at the upper part of the interventricular septum. The root of the aorta was slightly atheromatous, and the openings of both coronary arteries were involved. The coronary arteries themselves were distinctly thickened, but in no place calcareous or stenotic.

Their lumen was enlarged if at all altered. The aortic leaflets were slightly diseased but not calcareous. The valve seemed to be competent.

The lesion of importance was one on the anterior mitral leaflet toward its base and aortic edge. This was a patch of atheromatous character, sclerotic and white, and it extended to the endocardium exactly over the bundle of His where this band passes from the ventricle to the auricle. The relations were determined by removal

FIG. 2



Record of pulse, respirations, and temperature.

of the endocardium at the upper part of the interventricular septum. Viewed from the side of the right ventricle the specimen does not show any evidence of penetration of the sclerotic process, but on the left ventricular side it is evident that the bundle of His was involved in the area of disease.

The exact extent and relations of the pathological process cannot be stated until the histological studies now in course of completion are finished. These will be published in a subsequent paper.

The important fact in connection with the case is that the heart muscle was unaffected by any degeneration or sclerotic change excepting in the very limited area of the middle portion of the auriculoventricular bundle.

REVIEWS.

MANUAL OF ANTENATAL PATHOLOGY AND HYGIENE. THE FETUS. By J. W. BALLANTYNE, M.D., F.R.C.P.E., F.R.S.Edin., Lecturer on Midwifery and Gynecology, Medical College for Women, Edinburgh; Lecturer on Antenatal Pathology and Teratology in the University of Edinburgh (1900); Examiner in Midwifery in the University of Edinburgh; Assistant Physician, Royal Maternity Hospital, Edinburgh; Honorary Fellow of the Glasgow Obstetrical and Gynecological Society, and of the American Association of Obstetricians and Gynecologists. Edinburgh: William Green & Sons, 1902.

THE name of the author of this valuable book has become familiar through his studies in the difficult field of embryonal and fetal pathology. For this he has had especial advantages in being able to examine large numbers of specimens, while his consecutive study of the subject has added constantly to the interest and accuracy of his observations.

The work under discussion begins with a definition of the relation existing between antenatal and postnatal pathology. The author considers the antenatal factor in gynecological pathology and finds in this a reason, if possible, of such disorders. He draws attention to the effect of traumatism in birth and describes fully what he terms the physiological readjustment which takes place after birth.

Under the head of intranatal traumatism the author describes cephalhæmatoma, facial paralysis, fractures, and dislocations. In treating intranatal infections he believes that gonorrhœal ophthalmia should be anticipated and prevented by treatment during pregnancy. In our observation such treatment can be completely successful, although the mother's gonorrhœa may be of the most pronounced and virulent type. In the author's observation the absence of vernix caseosa has seemed to expose the infant to increased danger of mastitis.

Under the title "Scourge of St. Kilda" an interesting description is given of tetanus of the newborn in this island, and the tracing of its origin to infection of the umbilical cord; when antiseptic measures were employed in treating the umbilicus the scourge ceased. The author calls attention to the fact that the germs which produce septic infection in the newborn are everywhere present, and that

it is not remarkable that such infection arises, but rather strange that it does not more often happen. He urges thorough general precautions in the care of all infants. The etiology of hæmoglobinuria remains to the author in doubt, although the evidence of infection in these cases predominates. Under the head of Omphalorrhagia the author describes what seems to us septic infection of the umbilicus. This might have been to greater advantage described in connection with other septic processes.

Under the title of Neonatal Readjustments the author describes icterus, melæna, keratolysis, pemphigus, and sclerema.

In considering the pathology and hygiene of the fetus the author calls attention to the neofetal period during which the placenta is being established. He describes the growth of the fetus as most active if weighed between the fourth and fifth months, when the placenta is being fully established; placental weight corresponds to fetal weight. The author adds a scheme and diagram illustrating the development of the various organs.

In considering the anatomy of the fetus illustrations are given of sections through the cranium, thorax, abdomen, and pelvis; many of these are in colors; while they are not remarkable for excellence as illustrations, they aid considerably in elucidating the text.

The author describes the syncytium as a layer of nucleated protoplasm covering the villi of the full term placenta.

The fetal circulation receives full discussion, and the blood of the child is described at considerable length. The excess of leukocytes in the blood coming from the mother indicates a migration of white corpuscles from the maternal to the fetal blood, which may be a phase of fetal nutrition. In describing fœtal respiration, respiratory movements are recognized as occurring in utero.

The chemistry of the placenta and of the fetal excretions receives adequate treatment, while the functions of the ductless glands of the fetus are described.

In fetal pathology the author makes a minute classification, commencing with those disorders which are transmitted from the mother. He rightly emphasizes the importance of the placenta and membranes in studying the fetal body. A given specimen is certainly incomplete without fetus and membranes, and no autopsy upon the fetus alone without examination of these important structures can be conclusive. The infections transmitted from mother to child are fully described and every possibility considered is fully demonstrated. While fetal tuberculosis is rare, the author believes that about twelve instances of tuberculosis without lesion are recorded. The absence of tuberculous infection arises from the successful barriers to infection afforded by the placenta and the fetal liver. The author believes that tuberculous parents frequently have children who are malformed and cites the instance of a child born of a tuberculous mother who had web toes. Rheu-

matic fever is considered as one of the fetal diseases arising from transmission from the mother.

The author discusses fetal syphilis very fully and considers Colles' law by no means absolute.

The toxicology of fetal disease is fully considered, and among other causes of fetal mortality working in tobacco is recognized.

The author believes it is possible for the mother to be seriously ill with diabetes, cancer, leukæmia, or other diseases, and even eclampsia, and for the fetus to be born living and well. He considers that it is exceptional to find the morbid maternal state reproduced in the fetus; here we cannot agree with him, as we have seen fetal deaths from toxæmia follow two weeks after the birth of a vigorous child from an eclamptic mother. The cystic diseases of the fetus and elephantiasis are grouped together as illustrating diseases of the connective tissue. The diseases of the fetal skin are described at length with illustrations.

The writer discusses diseases of the fetal skeleton, discussing some of the rarer forms and omitting some conditions which are not infrequent, such, for example, as rachitis in the fetus. Fetal ascites is fully described and illustrated and attention drawn to the condition as a symptom of important pathological states in the viscera of digestion. In discussing the heart and its disorders, atheroma and endocarditis are referred to transmitted infections.

In considering disorders of the pelvic viscera, the writer believes that there is a downward displacement of the uterus which frequently occurs soon after or at birth and which is distinct from elongation of the cervix.

In concluding the volume the author describes briefly the accidents and injuries sometimes seen at birth and gives ample space to the discussion of hydramnios. Fetal death is fully described and the possibility of fetal rigor mortis is admitted. A colored illustration shows some of the changes which the fetus undergoes during maceration. As regards treatment of fetal death, if the membranes are unruptured, the physician is advised to wait, allowing changes in the placenta, membranes, and uterine wall to take place, which will diminish the chance of sepsis and hemorrhage. If the membranes are ruptured, the indications for interference are more clear, but even then it is wiser, keeping the patient under observation, to wait until the beginning of uterine contractions.

While the use of the antepartum douche may be permitted, it must be employed with great caution.

The consideration of the symptoms and diagnosis of fetal conditions and a consideration of those measures best adapted to promoting a sound and healthy development of the fetus conclude the volume.

This excellent work gives all the light available upon one of the darkest portions of pathology. Its practical value is great, for it

explains many phenomena not uncommonly observed in obstetric practice, and gives a rational basis for some important decisions regarding the treatment of the mother in the interest of the child. No one can rightly decide upon the various obstetric operations whose purpose is to save the life of the child without understanding sufficient of the conditions which make this life possible to choose wisely. While obstetric surgery is rapidly advancing and obstetric operations are more and more successful, they will frequently fail unless performed in cases where the child is in good condition. To recognize the fetal condition a knowledge of its physiology and pathology is of the greatest value.

It was our purpose to review with this the author's more recent volume on the pathology and hygiene of the embryo, which completes the entire subject, but this journal has not received this volume for review. E. P. D.

L'OEUF HUMAIN ET LES PREMIERS STADES DE SON DEVELOPPEMENT. Element d'embryogene par T. POTOCKI et A. BRANCA. Avec 100 figures et 7 planches. Paris: G. Steinheil, editeur, 1905.

THIS book of 196 pages has been written to serve as an introduction to the study of obstetrics, and does not pretend to be a treatise on embryology. The authors start with the intention of following the development of the ovum and of the fetal membranes in man alone. The great difficulty in such a study of making certain points clear without reference to comparative embryology is immediately apparent; so that even with their fixed purpose in view the authors continually revert to the development of the lower animals in describing the changes in growth of the human embryo. But since these references to comparative embryology are curt and introduced rather apologetically one feels only half enlightened upon certain parts of the subject. In their treatment the authors consider in turn "the sexual products," their origin and their morphological value; "the genital apparatus and the sexual life," ovulation and the corpus luteum, menstruation, the genital organs during pregnancy, the genital apparatus, and the postpartum; "the first stages of development of the embryo," fecundation, the segmentation of the egg, the formation of the embryonic membranes; "the embryonic membranes," the umbilical vesicle, the amnion, the allantois, the chorion, the fixation of the ovum and placentation, the umbilical cord. The book is well illustrated with figures, and contains seven rather familiar but well-executed plates representing in a schematic form the development of the fetal membranes. By reason of the large print and short paragraphing, so typical of the French, the book makes easy reading, and is on the whole interesting as an introduction to obstetrics. W. T. L.

STUDIES IN GENERAL PHYSIOLOGY. By JACQUES LOEB, formerly of the Department of Physiology, now Professor of Physiology in the University of California. The Decennial Publications, second series, Vol. XV. Chicago: The University of Chicago Press, 1905.

THE decennial publications from the University of Chicago are now well known to the general medical public. The present volume comprises a notable series of papers. Professor Loeb's unusual work in physiology has had wide recognition, and most of the articles which have been gathered together to form these volumes are already familiar to many whose immediate line of investigation lies outside of physiology. Practically all of Professor Loeb's original contributions have been collected and bound together to form the two volumes. There are thirty-eight papers, a large number of which appeared originally in German, and have been translated for this publication. In the first volume are the earlier articles dealing with the subject of heleotropism, while in the second volume one finds the well-known experiments on artificial pathogenesis. It is not, however, necessary to discuss the various subjects in detail. It is highly satisfactory to have these papers put into an accessible form, and for this one is indebted to the decennial publications. W. T. L.

ANATOMIE DES MEMBRES. DISSECTION. ANATOMIE TOPOGRAPHIQUE Par le DR. CH. DUJARIER, ancien prosecteur à l'Amphithèatre de Clamart, chef de clinique chirurgicale à la faculté. Avec 58, planches originales dessinées par Reignier. G. Steinheil, editeur, Paris, 1904.

UNDER this title M. Dujarier publishes an atlas which is "the fruit of his years as prosector in the amphitheatre of anatomy of Clamart." The book is intended for guidance of students in the dissecting room, placing beneath their eyes types of anatomical preparations which have been drawn by Reignier from specimens dissected by the author. There are 58 original plates, mostly in colors, illustrating the different steps in the dissection of the various parts of the limbs. Anomalies which are frequently encountered have been inserted. In addition to these plates there are 19 taken from Farabeuf. In the text each region is described with a little more detail than is usual in an atlas in order that the student will not be obliged to have recourse to a descriptive anatomy for a complete account of the structures. The author has particularly developed the chapters on the axilla, fold of the elbow, palm of the hand, region of the buttock, Scarpa's triangle, knee-joint, and sole of the foot. The book is clear and accurate and is recommended not only to students, but also to physicians who may at a glance desire to refresh their memory of the anatomy of the extremities. F. T. S.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

REGIUS PROFESSOR OF MEDICINE, OXFORD, ENGLAND,

AND

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

Meningismus Typhosus and Meningotyphus.—STAUBLI (*Deutsch. Arch. f. klin. Med.*, 1904, Band lxxxii. p. 90). Curschmann, in 1886, published 5 cases of genuine purulent meningitis complicating typhoid fever, and in his article draws attention especially to cases of typhoid setting in with signs of meningeal irritation, which, however, at the end of a week or two recede to give place to the usual symptoms of the disease. Fritz had previously noted similar cases and had pointed out that occasionally the meningeal symptoms persisted until late in the disease. He also emphasized the fact that such cases dying and coming to autopsy showed no lesion of the cord or brain. Since then many authors have commented on the condition, and in 1888 Wolf published 12 cases from Curschmann's clinic, 3 of which died, yet at autopsy the brain and cord were found to be normal, while cultures from the central nervous system were negative. Such instances have been explained by the presence of a soluble toxin with special affinity for the nerve cells. Stäubli cites 2 cases from Müller's clinic. In the first, with marked meningeal symptoms, no organisms were obtained by cultures from the spinal fluid, and after death the central nervous system showed no lesions. In the second there were, besides meningeal symptoms, motor cortical aphasia and ataxia of the legs and arms. This patient made a complete recovery. For such cases Bouchut has suggested the name "meningismus typhosus."

There are, however, cases in which at autopsy a purulent meningitis is found to explain the symptoms. Birch-Hirschfeld points out that brains showing apparently only a congestive hyperæmia may, on microscopic examination, display the early changes of inflammation. It was

for a long time contended that the typhoid bacillus could not produce a purulent inflammation and that the meningitis when present was caused by a secondary infection. There are now, however, numerous instances where the typhoid bacillus alone has been cultivated from the spinal fluid obtained during life and from the exudate after death. It would not be surprising if one could occasionally obtain typhoid bacilli from the brain, considering how widely distributed they are in the body, and to render the evidence conclusive they should be demonstrated in the exudate in sections. Stäubli offers such convincing evidence in a case he reports.

Enterogenous Cyanosis.—Hijmans v. d. Bergh (*Deutsch. Arch. f. klin. Med.*, 1905, Band lxxxiii. p. 86). In 1902 Stokvis described a new clinical picture under the name "Autotoxische Enterogene Cyanose." His patient, a man, aged thirty-eight years, had severe enteritis, clubbed fingers, and a very remarkable degree of cyanosis of the skin and mucous membranes, spectroscopic examination of the mucous membranes showing definite methæmoglobin bands. The similarity of the condition to poisoning with certain drugs, as with potassium chlorate and the aniline derivatives, led Stokvis to assume the development in the diseased bowel of some poisonous substance, which, when absorbed, converted part of the hæmoglobin into methæmoglobin. In the same year Talma reported 3 more cases, all with diarrhœa, clubbed fingers, intense cyanosis of the skin, and mucous membranes and methæmoglobinæmia. He demonstrated the characteristic spectral bands in the blood taken from the finger, as well as in the skin and mucous membranes, and showed further that the methæmoglobin was not free in the plasma, but remained attached to the corpuscles. To these observations v. d. Bergh adds two of his own.

His first case is that of a boy, aged nine years, who was born with atresia ani, which was operated upon. At the end of several months a rectourethral fistula formed, and since then has remained patent, so that feces and urine are both emptied through the bowel. For four or five years the mother had noticed that on exertion the child became cyanosed, and for a year previous to admission he had been blue, even while at rest. The poorly developed, emaciated child showed an intense cyanosis, which varied from day to day, but was always deeper after exertion. Heart and lungs showed no evidence of disease. In the rectum was a fibrous stricture, and above this a rectourethral fistula. At times fecal material could be pressed from the penis, but by catheterization urine was obtained, which was pale, cloudy, free from albumin and sugar, but contained much indol. Stools were frequent, thin, alkaline, with strong ammoniacal odor, and turned black on exposure to air. Spectroscopic examination showed the presence of a substance giving a band in the red, which was at first assumed to be methæmoglobin.

Considering such cases as evidently of toxic origin, attempts have been made to isolate the poison in the urine. Stokvis found that the urine after undergoing alkaline decomposition turned a deep red color on the addition of mineral acid, and rapidly converted oxyhæmoglobin into methæmoglobin, properties which the voided acid urine did not

have. Steensma has since shown that all urines which have stood any length of time give the color reaction above noted and convert hæmoglobin into methæmoglobin through the formation of nitrites, while the addition of a small amount of nitrite to fresh urine gives it these properties at once.

Oxyhæmoglobin converted by the urine of v. d. Bergh's case gave also a typical methæmoglobin band, but, to his surprise, on careful comparison, the band from the blood was placed a little to one side of this. Portions of the patient's stool mixed with normal blood gave this band, and v. d. Bergh concluded that the substance could not be true methæmoglobin and that the poison, whatever it may be, is not eliminated in the urine. After trying the action of numerous chemical agents on normal oxyhæmoglobin, he found that only hydrogen sulphide gas would produce a substance with an identical spectroscopic picture. Cultures from the stools showed a hydrogen sulphide producing bacterium, and this planted in a normal oxyhæmoglobin solution caused the same change. The effects of hydrogen sulphide gas on oxyhæmoglobin had previously been carefully studied by Hoppe-Seyler and Harnack, and the substance formed was called sulphohæmoglobin. This gives a distinctive spectroscopic picture which no other hæmoglobin derivative simulates, and corresponds exactly with that produced by the blood of the patient.

There is nothing in the literature concerning autointoxication from the gradual absorption of hydrogen sulphide from the intestines. While Bergeon's method of inflating the rectum of tuberculous patients with hydrogen sulphide gas was in vogue no spectroscopic examinations of blood were made. In animals the administration of Schlipp's salts causes sulphohæmoglobinæmia, while inhalation of the gas does not. Meyer has poisoned rabbits by directing a flow of H_2S into the intestines. It is difficult to see why in this special case there should have been any absorption of hydrogen sulphide with poisoning, and why in so many others where the gas is formed it should lead to no toxic symptoms. v. d. Bergh points out that the two most important factors in abnormal absorption were present, stagnation of intestinal contents and dilatation of the intestinal walls.

The second case reported is one of true methæmoglobinæmia. The patient, aged twenty-five years, was admitted for acute nephritis. He presented an intense grade of cyanosis, which had come on suddenly seven years before. His blood gave the typical reaction for methæmoglobinæmia. Intestinal symptoms were much milder than in previously reported cases. The cyanosis, too, was very variable, always deeper in the evening, irrespective of rest on exertion, and showing a remarkable relation to diet. An absolute milk diet for two days caused the cyanosis to disappear entirely, only to return with its former intensity after the first mixed meal. Meat seemed to exercise the strongest influence upon it.

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSISTANT SURGEON TO THE UNIVERSITY AND PHILADELPHIA HOSPITALS, AND ASSISTANT INSTRUCTOR IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA.

Some Surgical Notes on Tuberculosis of the Kidney.—KELLY (*British Medical Journal*, June 17, 1905, p. 1319) has never seen a case of primary ascending tuberculosis in upward of 50 surgical cases, for the most part in women; although he has seen several cases of vesical tuberculosis, primary or associated with a genital tuberculosis, but the kidneys were not involved. He has also seen coincident renal and genital tuberculosis, but without other manifest connection than the vascular system or some remote depot of infection. Without any doubt the infection of the kidney is almost always hæmatogenous, the primary focus being often in the thorax, sometimes in a cheesy bronchial gland apparently dormant. Therefore, in searching for evidence of latent disease, the lungs should always be examined carefully, and the region of the lymphatic glands of the neck should be searched for swelling and scars, as well as joints for old troubles. Tuberculosis once started in the kidney is almost always progressive, a spontaneous cure being exceedingly rare.

The real crux of the situation is the diagnosis. It is satisfactorily made when tubercle bacilli are found in the urine at more than one examination, and preferably by more than one observer, and when these are traced upward to the kidney and positively excluded from the other. In all obscure cases two guinea-pigs should be injected, one into the peritoneum, the other into the axilla. In three weeks the disease will have developed if present. The injection of tuberculin is valuable if, in addition to the general reaction, there is a marked local reaction in the form of pain in the kidney. A practised examiner will, in these early cases, find a slight thickening or hardening of the ureter on one side. An inspection of the ureteral orifices will often disclose a tell-tale blush or puffiness or granular condition. Any slight persistent cystitis rebellious to treatment should always be suspected as tuberculosis, and in such a case the diagnosis must be looked upon as incomplete until the condition of the kidney has been investigated. Cystoscopic examination is very valuable, often showing an ulcerated, suppurating, bleeding bladder. Involvement of only one ureteral orifice promises well, and renders useless the catheterization of the sound ureter, although Kelly has never seen any harm come from it.

Radical treatment, the extirpation of the disease in every case that will permit it, is the rule; but the other kidney must have been proven capable of sustaining life by a thorough analysis of the separated

urines. The diseased area should be excised only in rare cases in which it was evidently limited to one pole, as demonstrated by splitting the kidney from pole to pole and down to the pelvis, as it lay outside the abdomen before ligation and detachment. Nephrectomy, except as a preliminary to a radical operation, has proven to be an operation of necessity, not of election. When it is performed, all abscesses in both poles of the kidney should be opened.

Caution is advised before adding the ureteral extirpation to that of the kidney. The cases best adapted to the radical operation are those with a greatly enlarged, often strictured ureter. Involvement of the vesical walls has always been deemed one of the most serious local extensions of the disease, and by a number of surgeons is considered beyond the pale of surgical relief. The steps to be followed in these bad cases are: 1. Drain a bladder thoroughly. 2. Then remove kidney and ureter. 3. Use the prolonged bath at even temperature of 100° for hours or all day. 4. Close the fistula. 5. Treat any remaining small patches of disease with nitrate of silver, applied through the open-air speculum. 6. Use distention and irrigation treatments. 7. Excise any rebellious areas of the disease.

The small patches of disease around the ureteral orifice are rarely tuberculous, and this is the reason why they clear up readily without further treatment after nephrectomy.

Concerning the Subcutaneous Transference of the Omentum.—NARATH (*Zentralblatt f. Chirurgie*, August 12, 1905) says that the last word has not been said of the Talma operation. While it is doubtful whether the operation has influenced favorably the diseased process in the liver itself, it is certain that it is followed sooner or later by a disappearance of the ascites and some of the disturbances of which the patients complain, and that the patients feel well again and are able to work. Of the abdominal organs which can be fixed to the abdominal wall, the omentum and spleen deserve special mention. The cases in which the spleen can be sutured to the abdominal wall will not be particularly numerous, since we do not care to burden with further disturbances patients who are already very miserable.

The fixation of the omentum has been attempted by very different methods. One should give that method the preference which can be carried out most simply and without narcosis. Narath has concluded after repeated trials that it is best to suture the omentum in a subcutaneous pouch in the anterior abdominal wall. He says that this method produces an abundant anastomosis.

The technique is as follows: 1. Under Schleich's method of local anæsthesia the abdomen is opened in the median line, just above the umbilicus, to the left of the round ligament, thus sparing the paraumbilical veins as much as possible. 2. The abdominal incision should not be unnecessarily large, lest the intestine escape through the wound alongside the omentum. The ascitic fluid should be thoroughly evacuated from all the dependent parts, siphoning it out by tubing if necessary. 3. A thick end of the great omentum is then seized and drawn out of the wound without disturbing the transverse colon from its natural position. This part of the omentum should contain as many large bloodvessels as possible, and at the level of the umbilicus should be of one to two fingers' thickness. 4. The abdominal wall should now

be closed about the omental stump without compressing the omentum, which should come through in a direct line. 5. The omentum is then fixed to the parietal peritoneum and linea alba by a few fine sutures, avoiding the veins. 6. The omentum outside the abdomen is then lodged in an oblique pouch in the subcutaneous tissues, about 15 cm. long, and directed to the left of the median line. 7. A water-tight closure of the skin wound should be made and a bandage applied that will not compress the subcutaneously situated omentum.

In the next few days there is observed an œdema of the abdominal skin, probably due to an escape of ascitic fluid. Later this disappears, and in about eight days a radiating group of small veins are seen, while the larger veins increase in size. The displaced omentum becomes distinctly swollen and the veins filled to their utmost. The degree of venous dilatation differs individually very much. Narath has seen some veins in the abdominal wall swollen to the size of the thumb.

An occasional danger comes from the slipping alongside the omentum through the abdominal incision of a portion of the transverse colon or small intestine to a subcutaneous position. This is due to faulty technique in the closing of the wound about the stalk of the omentum.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

PROFESSOR OF MEDICINE AND THERAPEUTICS AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; VISITING PHYSICIAN TO ST. MARK'S HOSPITAL.

ASSISTED BY

HENRY HUBBARD PELTON, A.M., M.D.,

ASSISTANT PHYSICIAN TO THE PRESBYTERIAN HOSPITAL (OUT-PATIENT DEPARTMENT), NEW YORK.

Absorption, Elimination, and Mode of Action of the Quinine Salts.—Dr. Armaud has concluded from observations of the physiological action and elimination through the urinary tract that, in individuals without febrile movement, quinine is present in the circulation in from six to nine hours after administration; in febrile conditions it is absorbed after from nine to twelve hours. The dosage being equal, elimination takes place more rapidly in subjects who have taken the drug for some time, since the organism, already saturated, throws off the greater part of the quinine ingested; consequently the greater the dosage the more of the drug will be eliminated. Reduction of the dose renders assimilation more free, retards its elimination, and reduces the quantity of quinine in the free circulation. The therapeutic action depends rather upon the amount of the drug in the circulation than upon the quantity assimilated by the tissues. The action of quinine, then, should depend upon the amount taken and its maximum effect coincide with the presence of the maximum amount free in the blood current; that is,

about six to nine hours after ingestion in the afebrile individual and from nine to twelve hours in fever patients.—*Marseille médicale*, 1905, No. 11, p. 356.

Thiosinamine Injection in Cicatricial Œsophageal Stricture.—Dr. Karl Schneider reports a case of cicatricial stricture of the œsophagus following the ingestion of caustic soda in a child of five years; the œsophagus of the patient after the initial inflammation was healed would allow the passage of a No. 24 (F.) sound. The child was not seen for five months, and at the next observation the obstruction prevented the passage of the finest bougie. Injections of thiosinamine, 1 part; glycerin, 4 parts; water, 16 parts; 10 minims were prescribed. After two injections three days apart a No. 9 (F.) sound could easily be passed. The quantity of the injection was raised to 15 minims, the treatment was continued, and in about two weeks the stricture would admit a No. 28 (F.) sound.—*Correspondenz-Blatt f. Schweizer Aerzte*, 1905, No. 11, p. 356.

Aristochine in Whooping-cough.—Dr. H. Koppe advocates the employment of this drug in pertussis. At first it is administered only once or twice daily, but after a few days the patient should receive from three to five doses during the twenty-four hours. The dosage for children under a year old is from 3 to 4 grains; for those beyond this age 7½ grains at a time, given in sugar or with the pulp of fruit; a short time afterward the patient should receive a few drops of diluted hydrochloric acid well diluted with water (this should be taken through a tube to save the teeth); the author has never known the drug to cause unpleasant sequelæ.—*Deutsche Aerzte-Zeitung*, 1905, No. 9, p. 201.

The Treatment of Capillary Bronchitis in Children.—Dr. Schopohl advocates the employment of baths at 96.8° to 100.4°, increased gradually to 104° to 113°, and lasting ten to twenty minutes. To maintain the resulting cutaneous congestion the patient is wrapped, without being dried, in a sheet; outside this a covering of linen fabric is applied and the child allowed to rest for an hour or two; he is then unwrapped and the chest enveloped in oil silk, the dressed side of which has been smeared with warm oil. One such procedure usually suffices to greatly improve the patient's condition, but in severe cases it may be necessary to employ it twice during the same day. As an adjunct to this treatment the continuous inhalation of steam is recommended. The author considers that his method lessens the intrapulmonary congestion, increases the excretion of urine, relieves the overacting heart, and brings about a general improvement.—*Blätter f. klin. Hydrotherapie*, 1905, No. 4, p. 80.

Hereditary Syphilis in Infants.—Dr. B. Salge considers the prognosis favorable in those cases in which symptoms, coryza, etc., are manifested six weeks or so after birth. He disapproves of the treatment by baths in bichloride solution on the ground that there is no means of ascertaining how much of the drug is absorbed and because their action is not rapid unless the skin is scarified. He considers inunctions and the internal administration of mercury, in the form of calomel or the yellow iodide, preferable. The most efficacious method, however, is, in his

opinion, that by hypodermic injection. He uses the following formula: Mercury bichloride and sodium chloride, of each 0.2 part; water, 10 parts. Of this solution one-tenth of the content of a Pravaz syringe is injected into the substance of the muscles once a week. The treatment is but slightly painful and is very efficacious. For the syphilitic coryza the author employs insufflations of 1 part of calomel to 20 parts of sugar, applications of red mercuric oxide upon bits of cotton, and a spray of adrenalin chloride. If bloody stools with mucus occur the treatment is stopped. The fact that specific disease interferes to a marked degree with the nutrition and development of the child makes energetic treatment necessary. The preferable food for these children is, of course, breast milk.—*Berliner klin. Wochenschrift*, 1905, No. 22, p. 690.

Marmorek's Serum in Tuberculosis.—Dr. T. Stephanie has used this substance in the treatment of 7 cases, in 2 of which he achieved rather remarkable results. He concludes that in this remedy we have a powerful agent in the treatment of tuberculous conditions, both intrapulmonary and extrapulmonary, and one which is, in general, harmless. Not only is it potent in recent cases, but in those of long standing as well, in which other methods of treatment have proved of little avail. He expects to continue its use in his practice and believes those in such diseases as that due to the bacillus of Koch, while our resources in the combat against them are all too few, we should omit no form of treatment which may possibly result in benefit to the patient.—*Le Progrès médicale*, 1905, No. 25, p. 393.

The Treatment of Jaundice.—Drs. H. Huchard and C. Fiessinger vary the treatment of this condition in accordance with its causation; in all cases, however, a milk diet is necessary—a tumblerful every four hours, with the addition of a little alkaline water, lime-water or Vichy. The alkaline mineral waters and infusions, such as aniseed tea, may be allowed. The bowels should be opened by sodium sulphate or other mild alkaline; calomel is neither effectual nor well borne; intestinal antiseptics, salol, naphthol, etc., should not be given. Intestinal irrigations, when there is intestinal colic, are indicated; a quart of hot or cold water may be given in this manner morning and evening. The saline laxative should be continued for a week, then omitted for a week, during which 15 grains of sodium benzoate or salicylate are administered at noon and evening. The morning laxative may be replaced by a pill of euonymin, gr. $\frac{1}{4}$; podophyllin and belladonna extract, each gr. $\frac{1}{8}$. The milk diet should be continued, and to it may be added a little macaroni or vegetable purée soup. In tertiary syphilitic jaundice specific treatment is indicated. Pruritus may be relieved by alkaline baths, warm douches, a warm lotion of coal tar, $\frac{1}{2}$ ounce to the quart of water, weak solutions of carbolic acid, mercury bichloride, 1 : 2000, ichthyol, mentholated talcum powder, etc. If it is obstinate the skin may be dressed with ichthyol, 10 parts; alcohol and ether, each 50 parts, followed by a soothing powder, or by glycerin, 20 parts, to chloroform, 60 parts. In icterus due to gallstones, a course of spa treatment may prove effectual, or this failing, surgical intervention may be considered. If symptoms of cholæmia appear the milk diet is necessary and an enema should be given each morning, to be followed after an hour by an irrigation of 8

ounces of saline solution; about 3 ounces of macerated pork liver should be given daily mixed with a little water. The nervous symptoms may be relieved by packing in a sheet wrung out in water at 100.5° twice a day or by two or three baths daily at from 82° to 86° and lasting ten or fifteen minutes.—*Journal des praticiens*, 1905, No. 23, p. 361.

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE; PROFESSOR OF OBSTETRICS AND DISEASES OF INFANCY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE WOMAN'S MEDICAL COLLEGE; VISITING OBSTETRICIAN TO THE PHILADELPHIA HOSPITAL, ETC.

Puerperal Endocarditis.—In the *Monatsschrift für Geburtshülfe*, 1905, Band xxi., Heft 5, WINKLER reports the case of a patient who was delivered of a living child in spontaneous labor; the afterbirth was also expelled spontaneously. Fourteen days after labor the patient had fever, with swelling of the joints of the right hand and then of the right foot. An eruption appeared on the face, which spread over the entire head. The patient was admitted to the hospital and was treated by inunction and developed the characteristic temperature of pyæmia. The pelvic organs were normal, but endocarditis developed. The patient developed cyanosis, with high fever, chills, and died in collapse.

Upon autopsy the pelvic organs were normal, but endocarditis was fully developed. In the joints were found foci of infection. The exciting cause of the infection and the nature of the infective germ were not discovered.

Ileus in the Puerperal Period Successfully Treated by Eserin.—KREBS (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1905, Band xxi., Heft 5) reports the case of a multipara, who, three and a half days after a normal labor, developed abdominal distention and vomiting of bile, and normal pulse and temperature. There was no hernia, and the uterus was not retroverted, nor could a tumor be found. During the last months of her pregnancy the patient had vomited frequently.

An affort was made to move the bowels by injection, but without success; 1 mg. of eserin salicylate was given hypodermically. Half an hour later peristalsis began, gas escaped from the bowel, and three-quarters of an hour later the patient's bowels moved several times. She made a good recovery.

The Nature of Hæmatoma of the Muscles of the Neck in the Newborn.—In the *Zentralblatt für Gynäkologie*, 1905, No. 20, PINCUS reports the case of a child born in spontaneous labor who died fourteen days after birth. There was no history of syphilis in the parents. Two days after delivery the child developed on the left side of the neck a hæmatoma

of the sternocleidomastoid muscle. On microscopic examination of this tumor, a fibrous myositis was present. This evidently was of a progressive nature, and would have involved a considerable portion of the muscle. It was interesting to observe that blood pigment was entirely lacking, and that also connective tissue was absent from the tumor.

Two Cases of Hebotomy.—SCHAUTA (*Zentralblatt für Gynäkologie*, 1905, No. 20) reports the case of a primipara, aged twenty-three years, with contracted pelvis, mitral insufficiency, and albumin in the urine. The child was presenting in brow presentation; although the pains were good, there was no progress. The patient had been examined before admission to the hospital, and antiseptic precautions had not been strictly observed. The child was living, although the head had not engaged.

In view of the fact that the patient had been examined without rigorous antisepsis, Cæsarean section was declined, and the pelvis was opened on the left of the median line by hebotomy; the forceps was then applied and a living child delivered. Hemorrhage was controlled by tampon, and the wound was closed by drainage. Mother and child made a good recovery, and the pelvis showed good bony union.

He also reports the case of a multipara with contracted pelvis in whom hebotomy was done because the head failed to engage. Delivery was effected by use of forceps, and mother and child recovered well. There was no hemorrhage nor other complications.

Rupture of the Cervix by a Metal Dilator.—BURGER (*Zentralblatt für Gynäkologie*, 1905, No. 19) reports the case of a primipara, aged forty years, in the eighth month of pregnancy, who had eclampsia and had had twenty severe paroxysms. The cervix was 4 cm. long and admitted one finger only; Frommer's dilator was used, and all possible care was exercised in dilating slowly. In fifty-five minutes dilatation had proceeded to No. 7, when it was found that the branches of the instrument had penetrated deeply into the cervix, and that on the left side of the cervix there was occurring free hemorrhage. On removing the instrument it was found that a laceration, between 6 and 7 cm. long, was present at this point; craniotomy was performed, the uterus emptied, and the tear in the cervix closed. The patient died eight hours later from eclampsia. Autopsy showed cerebral hemorrhage, with œdema and hemorrhage in the pleura and liver. The tear in the cervix was found to be 8.5 cm. long and 4 cm. wide. There was no evidence that it opened the peritoneum, as muscular tissue was found throughout the extent of the tear.

Persistent Posterior Rotation of the Chin.—In the *American Journal of Obstetrics* for May, 1905, REED reviews thoroughly this subject, and arrives at the following conclusions:

In labor the face may reach the pelvic floor without anterior rotation of the chin. In most cases, however, anterior rotation does occur spontaneously; when it does not interference is indicated. The child's neck is sufficiently long to permit the head to sink deeply into the pelvis before the thorax is involved. In 22.6 per cent. of cases the chin was delivered without rotation; the maternal mortality of these cases was

practically that of placenta prævia under aseptic conditions, namely, 12 per cent. The fetal mortality is about that of eclampsia under modern methods of treatment.

If the head is not engaged, an effort should be made to produce flexion by the hand, if this fails version should be performed. If the head has engaged, an effort should still be made to produce rotation by the hand. If forceps are used at all, it should be as a last resort before embryotomy. Fetal mortality under the use of forceps is 50 per cent.; only axis traction instruments should be used. If symphyseotomy be elected, it should be performed when the child is vigorous enough to justify the operation.

Puerperal Septic Infection.—The *Practitioner* for March, 1905, is devoted to the discussion of puerperal septic infection. Herman writes upon clinical phenomena, describes the puerperal ulcer, hospital gangrene, spreading traumatic gangrene, sapræmia, septicæmia, pyæmia, peritonitis, late peritonitis, and pelvic cellulitis as different forms of the disease.

Galabin describes the treatment and has found advantage in obtaining material from the uterus for examination in employing the double sterilized tube. The outer and larger tube is closed at the end by a thin india-rubber diaphragm; when this is passed within the cervix the inner and thinner tube is pushed through, it takes up the secretion and is then withdrawn within the rubber.

The uterus is thoroughly irrigated with chinosol, 0.25 per cent.; tincture of iodine, 1 per cent, or lysol, 1 per cent. Vaginal douches of bichloride, 1: 3000 or 1: 4000, are often used. The bowels should be freely opened.

If this does not suffice, the uterus must be thoroughly explored by the finger; retained matter broken down and separated, and then removed by irrigation. If bleeding occurs, packing with iodoform gauze is indicated; suppositories of iodoform, each containing 2 drachms, may be introduced into the uterine cavity daily for some time.

Free feeding is advised, and normal salt solution beneath the skin; fever is to be reduced by cold and quinine and iron may be given; phenacetin for pain, and strychnine for feeble pulse was also recommended. Antistreptococcic serum has been of value in some of his cases.

The author speaks well of collargol, although he apparently has had no experience with that or with nuclein.

So far as operative treatment is concerned, he would limit this to the opening of abscesses; if such are pelvic, they should be opened through the vagina; if abdominal, they should be opened through the abdominal wall. Hysterectomy should very rarely be done, and then if the uterus is large, through the abdomen; and if it is small, through the vagina. Occasionally abdominal section affords a chance for recovery in peritonitis while opening the posterior cul-de-sac is useful in pelvic peritonitis, It is occasionally useful in beginning pelvic peritonitis.

The Prevention of Puerperal Septicæmia.—In the *Practitioner* for March, 1905, HART contributes a paper upon this subject. He lays especial stress upon the sanitary oversight of the patient during pregnancy, and upon the observance of such hygiene that shall bring her into the best possible condition. He urges cleanliness at the time of

labor with thorough disinfection of the hands, and believes that they can be made practically pure for obstetric work without the use of gloves. To one accustomed to operating with gloves there is no objection to their use, although they interfere with the sense of touch at first.

One thorough vaginal examination is usually sufficient and should be made with every precaution for surgical cleanliness. The course of labor should carefully be watched, and forceps should not be used too early nor too late. Deep lacerations should, if possible, be avoided.

He also urges that the placenta should not be delivered too early, and thinks that Credé's method has been harmful in this respect. Laceration of the cervix, giving rise to hemorrhage, should be sutured, and all except the slightest tears of the perineum should be closed. He gives one hot vaginal douche after labor, but no others.

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

OF NEW YORK.

Prolapsus Uteri in Virgins and Multiparæ.—ERTZBISCHOFF (*La gynécologie*, August, 1905) states that prolapsus may be found even in newborn infants, in whom there is nearly always an accompanying spina bifida. It is doubtless due to defective innervation of the uterine ligaments and pelvic muscles. In virgins and multiparæ the principal etiological factor is want of muscular tone, due either to vasomotor or atrophic conditions, to which are added repeated and severe bodily efforts.

The treatment varies according to the extent of the prolapsus. If slight it can be corrected by plastic operations on the vagina; a simple prolapsus without accompanying cystocele is best treated by hysteropexy combined with intra-abdominal shortening of the round ligaments. In complete procidentia in a young woman, hysteropexy and plastic operations are indicated, in an old subject supravaginal amputation of the uterus, with fixation of the stump to the abdominal wall, and accompanying colpoperineorrhaphy. All such operations should be supplemented by treatment directed toward improving the muscular tone of the patient.

Metritis in Virgins.—DALCHE (*Arch. de thérap.*, 1905, No. 4) believes that infection of the endometrium occurs not infrequently in young girls, due to bad hygiene or accidental blenorrhœal contamination, and is apt to be aggravated under the influence of menstrual congestion. The onset of the disease is more acute than in adults, being marked by severe pains in the hypogastric, ovarian, and sacral regions, accompanied by a mucopurulent discharge, menorrhagia, and metrorrhagia. On examination the cervix is found to be hypertrophied and eroded,

the corpus uteri being congested. In a variety described by Pozzi partial or complete arrest of the development of the uterus results.

The treatment consists in those of antiphlogistic remedies, leeching, hot baths, douches, and compresses over the abdomen. Curettement is indicated in cases of menorrhagia due to hyperplasia of the endometrium, dilatation with small laminaria tents in the atrophic variety.

Ovarian Fibromata.—PUECH (*Gazette des hôpitaux*, March 4 and 11, 1905) reviews this subject at length, with especial reference to the diagnosis, which he believes is seldom positively made before the abdomen is opened. A large fibroma of the ovary is apt to be mistaken for one of the uterus, a smaller tumor for a semisolid cyst or diseased adnexa. The mobility of the tumor, the absence of metrorrhagia, the small size of the uterus, and the presence of ascites, all speak in favor of an ovarian fibroid. Dermoid cysts are especially difficult to distinguish from the former. Papilloma is also readily mistaken for fibroma, as well as ectopic gestation.

The writer believes that one cannot affirm that a solid tumor of the ovary is not a sarcoma or carcinoma, but in any case an explorative incision is indicated.

Arterial Tension during the Climacteric.—PAWINSKI (*Gazeta lekarska; Zentralblatt f. Gynäkologie*, 1905, No. 33), as the result of observations in 375 cases, concludes that increased arterial tension is a common symptom of the menopause. It is often observed in women who still menstruate regularly, as well as after the flow has entirely ceased. It diminishes under the influence of profuse flow and nervous influences. This tension is the cause of the tachycardia as cardiac irregularity and so often observed in these subjects.

The climacteric has no particular influence upon the development of arteriosclerosis, though sternocardiac attacks often occur. If aortic lesions are present the heightened arterial tension has an unfavorable influence, but in mitral disease, with low blood pressure, the effect may sometimes be beneficial.

The writer finds that preparations of iodine are not borne well in patients with climacteric arterial tension. He administers ovariin and advises a diet of milk and vegetables.

Combination of Cancer and Fibromyoma of the Uterus.—PIQUAND (*Ann. de gyn. et d'obstétique*, July, 1905) concludes the first half of a paper on this subject as follows: 1. Cancerous degeneration of a fibromyoma is rare, although the writer has been able to collect 45 cases. 2. Usually the fibrous growth is invaded by cancer in the neighboring tissue (especially the endometrium), though exceptionally the original focus may be in the ovary. Cancerous emboli brought through the lymphatics into the tissue of a fibroid from distant organs have been described in only 3 instances. 3. The writer has found 24 authentic cases in which the fibromuscular elements seem to have been actually transformed into epithelial cells (?), though he admits that in some cases pre-existing cells are present in fibroids which may proliferate and develop into a malignant growth. These cells may be derived either from the embryonic remains of the canal of Wolff or Müller, or more frequently are simply epithelial ingrowths into the fibrous tissue

of the endometrium covering the neoplasm, which become isolated, multiply in an irregular manner, and finally develop into primary epithelioma.

Effect of Castration on the Sexual Function.—VINSBERG (*Revue d'obstétrique et de gynécologie*, 1905, No. 7) states that castration does not diminish sexual feeling in women; in fact, it is often increased in women with small, non-developed uteri.

He believes that removal of the uterus and adnexa has little influence of the function; on the contrary, increased passion was noted in several instances. Mandel and Burger, from a series of observations in 25 women, found that in 9 sexual feeling was diminished after castration, and in 6 it was abolished.

[We are more apt to regard the conclusions of the latter writers as more nearer the truth, judging from the extended results of our own practice and observation.—H. C. C.]

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

AND

MILTON B. HARTZELL, M.D.,

INSTRUCTOR IN DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

Treatment of Mycosis Fungoides by Radiotherapy.—BELOT and BRISSERIE (*Archives d'Electricite medicale*, November 25, 1904) speak of the good results obtained in two cases, one in the premycotic, the other in the fungoid stage. Low vacuum tubes were used (from 4 to 9 H., Holzknecht's chromoradiometer) at each sitting, and at intervals of fifteen or twenty days. Some tumors were removed by 9 H.; others required 35 to 40 H. in all, and sometimes one treatment produced good results. It is not regarded as desirable to cause inflammation. The itching is speedily relieved. The authors are of the opinion that the amount absorbed and the quality of the rays are important factors, but the apparatus employed and the distance of the tube from the skin are of small importance. In one case the treatment extended over a year, the patient increasing in weight during this period. In none of the cases of any disease treated have the authors ever observed any bad effect on the general health of the patient. [Like reports have been made by other observers, but in one case by the abstractor of the above article no benefit was derived by this treatment.]

Glandular and Cutaneous Diseases Healed by Radiotherapy.—R. H. BOGGS (*St. Louis Medical Review*, March 18, 1905) considers it unwise to apply *x*-rays to trivial diseases that can be cured by other less expen-

sive methods. The rays must be prescribed and given in a therapeutic dose for each disease, in order to obtain good results. Tissues are not always affected to the same extent by the same dose, any more than the same dose of a drug will always produce the same physiological effect. Idiosyncrasy is not believed to be a frequent cause of excessive inflammation, but a certain affected area of disease will react more readily than healthy tissue, because the life of the cells is lower. It requires twice as many units of *x*-radiation to produce the same degree of reaction in healthy tissue as it does in many forms of diseased tissue. If the dosage is small, causing stimulation, nutrition is improved, but if large, atrophy and degeneration in one form or another are liable to follow. The author states that 75 per cent. of acne cases can be cured without producing inflammation, but in the other 25 per cent. of cases reaction to the extent of desquamation (as in severe sunburn) is required. He considers that the benefit is due to an induced leukocytosis. [In extolling the *x*-rays for the treatment of this often trivial affection, we are surprised that the author does not caution the operator on the liability to the occurrence of the unpleasant results that may occur from short and infrequent exposures, especially in the form of persistent pigmentations and telangiectases, either of which (when they occur) may be most disfiguring and lasting than the acne.—Abstractor.] Attention is called to the good results in a few cases of Hodgkin's disease and in goitre. A remarkable improvement in the general health usually follows after a few radiations in the former disease, while in the latter the growths are not only reduced in size, but the symptoms of the disease often disappear.

Xanthoerythrodermia Perstans.—H. RADCLIFFE-CROCKER (*British Journal of Dermatology*, April, 1905), under the above provisional title, describes a form of disease which he believes has not been described hitherto. During the past three years he has observed 10 cases of the affection, all of them males, with one exception. Up to the present all the cases have been adults. The eruption begins as pale pink or yellowish patches on the limbs and trunk, the uncovered parts of the body being free or very slightly affected. The patches come out very gradually and in small numbers, being, as a rule, symmetrically placed. As the old patches do not entirely disappear and new ones are continually coming out, large areas are eventually involved. They are usually oval or elongated in shape, and arranged symmetrically on the back in the direction of the ribs, and often but not always in vertical lines on the limbs. Pinching up the skin reveals distinct infiltration, but the patches are not raised above the healthy skin. The surface is smooth on the trunk, but slightly rough or even scaly upon the limbs. The thighs are the parts most frequently first affected, next the legs, then the trunk; the face is nearly always free. In most cases itching is slight or absent. The duration of the disease varies from a few months to many years, and is apparently compatible with perfect health. The affection seems to be fairly amenable to treatment; 2 cases were cured and others improved by the administration of salicin internally and iodine vasogen locally. In the single case occurring in a female exposure to the Roentgen ray cleared up the affected area entirely. Nothing is known as to the etiology. Two of the patients had syphilis, but antisyphilitic treatment pursued vigorously for a year was without effect. Microscopic

examination of excised portions of skin showed absent or atrophied stratum granulosum, absent stratum lucidum, and slight œdema of the epidermis generally. The vessels of the corium were dilated and surrounded by some cellular infiltration. The collagen was apparently normal, with the exception of slight œdema, but there was apparently a reduction in the quantity of elastin, especially in the papillary layer.

OTOLOGY.

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

OF BOSTON, MASS.,

PROFESSOR OF OTOLOGY, HARVARD UNIVERSITY.

ASSISTED BY

W. A. LE COMPTE, M.D., E. D. WALES, M.D., AND D. H. WALKER, M.D.

Technique of and Indications for Removal of the Malleus and Incus.—HERNRICH NEUMANN (*Archiv f. Ohrenheilkunde*, Band lxiv.), under the above title, discusses the method of anæsthetization of the tympanum and tympanic membrane, the technique of the operation, and the indications for the operation itself. Neumann advises local anæsthesia by the method used in Politzer's clinic for all endotympanal operations. The fluid used for injection beneath the skin of the external auditory canal is a 1 per cent. solution of cocaine, to which tonogen, a preparation of adrenal extract, is added, in the proportion of 1 to 4 drops of tonogen to a cubic centimetre of the cocaine solution. The subcutaneous syringe used for the injection differs from an ordinary syringe, in that the needle is attached to the barrel at an obtuse angle, for ease in manipulation. The needle is introduced beneath the skin of the external auditory canal in its upper part and about 0.5 to 1 cm. outside of the place of juncture of the cartilaginous and bony portion of the canal and is carried in from this point under the periosteum of the bony canal. For satisfactory anæsthesia it is necessary to inject sufficient fluid to elevate the upper and posterior cutaneous lining of the bony canal. The efficacy of this method of cocainizing the tympanum and tympanic membrane is dependent upon the anatomical structure in this situation. The cutaneous lining of the bony canal in its upper part goes over directly into the epidermal layer of the pars flaccida of the tympanic membrane, and, as the pars flaccida has no membrana propria and its inner layer of mucous membrane is a direct continuation of the mucous membrane lining the tympanic cavity, the fluid injected will in part spread under the mucous membrane of this cavity. Sometimes a swelling of the mucous membrane over the promonotory can be observed when this method has been used. The injected fluid also penetrates along bloodvessels which pierce the outer wall of the attic, thus reaching the space of Prussak and the external attic wall. Another

anatomical factor in this location is the strand of connective tissue which is found at the point of union of the os tympanicum and the squamous portion of the temporal bone. This connective tissue is continuous with some of the mucous membrane reduplications of the tympanum. These facts serve to explain the manner in which, in a subperiosteal injection in the bony canal, the fluid reaches the mucous membrane of the tympanic cavity. At least ten minutes must elapse between the time of the injection and the beginning of the operation.

The extraction of the hammer is accomplished in the usual way. After severing the remnant of drum membrane up to either side of the handle of the hammer by means of a round-ended knife, a Delstanche ring knife embracing the handle is passed up as far as possible, severing the tensor tendon and other attachments. The extraction is then completed by means of Sexton's forceps. With these forceps the hammer is seized above the short process and drawn down and then out. After a hearing test the anvil is removed by passing a curette, the curette end of which is bent at an angle of 100 degrees with the handle, into the space previously occupied by the head of the hammer and then sweeping backward and downward with the concavity of the curette directed to enclose the anvil.

In cases where there is found to be purulent inflammation or cholesteatome formation in the attic, Neumann advises the removal of the external attic wall. Two parallel cuts beginning at the inner end 1 cm. long are made through the skin of the upper canal wall and their outer ends connected by a cross-incision. The skin between these incisions is then dissected up and removed. The outer attic wall is then denuded of skin and is removed with small chisels. This removal of the attic wall is quite painless with the local anæsthesia described above.

The indications for the extraction of the hammer and anvil depend on the nature of the suppurative process. Chronic suppuration in the attic when there is no symptom suggesting disease of the temporal bone is an indication for the removal of the ossicles, after a thorough trial of conservative treatment has proved unavailing. Cases of chronic suppurative middle-ear disease with perforation in the anterior segment of the drum membrane are not suitable for this operation, as they are almost never associated with caries of the ossicles. Neumann urges as a point in favor of performing the operation with local anæsthesia that in cases where there is only a suspected involvement of the temporal bone in the carious process (cases which, were the involvement of the temporal bone proven, would be suitable for complete exenteration), the extraction of the ossicles may be done as an exploratory operation without the patient, after undergoing, under general anæsthesia, an operation for removal of the ossicles, refusing, from dread of the anæsthesia, further necessary interference. The extraction of the ossicles, with removal of the outer attic wall, does away with the Stacke operation, since the cases, where extensive interference with the temporal bone is required, are more easily operable by the regular complete exenteration, and cases where this is not required are as satisfactorily treated by the simple removal of the ossicles and the outer attic wall.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

SIMON FLEXNER, M.D.,

DIRECTOR OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK.

ASSISTED BY

WARFIELD T. LONGCOPE, M.D.,

DIRECTOR OF AYER CLINICAL LABORATORY, PENNSYLVANIA HOSPITAL,

AND

G. CANBY ROBINSON, M.D.,

RESIDENT PATHOLOGIST, PENNSYLVANIA HOSPITAL, PHILADELPHIA.

The Function of the Interstitial Gland of the Testicle.—BOUIN and ANCEL (*Journ. de phys. et de pathologie gen.*, 1904, tome vi. pp. 1012 and 1039) publish two contributions on this subject. In the testicles of mammals one may distinguish three types of elements. 1. The seminal cells, which together constitute the seminal gland. 2. The cells of Sertoli, which form a nourishing syncytium for the seminal cells. 3. The large interstitial cells. Recent researches seem to show that these latter cells make up a special gland, and further work, which the authors have confirmed, suggests that at least one function of this interstitial gland is to participate in the nutrition of the seminiferous tubules. A much more important function, however, is the possible relation of the internal secretion from this gland to the sexual instinct of the male.

The cells of the seminal tubules have no general action, at least in animals, for the testicles in cryptorchids of the first order, animals which have normal sexual instincts, were found to contain no seminal cells, while the cells of Sertoli and interstitial cells were well developed. Experimental or pathological stenosis of the vas deferens in animals led in certain cases to complete degeneration and final loss of the seminal cells without, however, loss of sexual instinct. In these animals the cells of Sertoli and interstitial cells were not affected. After removal of one testicle and ligation of the vas deferens of the other the remaining organ showed a compensatory hypertrophy of the interstitial cells, with gradual atrophy and degeneration of the cells of Sertoli. With these changes there is no loss in sexual instinct. The authors believe, therefore, that the sexual instinct is entirely dependent upon an internal secretion elaborated by the interstitial cells of the testicles, the interstitial gland. Dissections upon embryo pigs showed that the growth of the sexual apparatus was dependent upon the development of the interstitial gland, and that the presence or absence of these cells determines the sex of the animal. The female genital gland presents no formation which is homologous to these cells at the same ontogenetic stage.

Finally, arrests in the function of the interstitial gland, demonstrable through lack of growth of the interstitial cells in the testicles of young animals, is accompanied by an arrest in development of the secondary sexual apparatus and the non-appearance of tertiary sexual characters.

The Origin of Acute Miliary Tuberculosis.—SILBERGLEITH (*Virchow Arch.*, 1905, Band clxxix. p. 283) reports the pathological findings from

31 cases of acute miliary tuberculosis, in 23 of which a focus of tuberculosis was carefully searched for in the blood and lymph vessels. In 22 of these cases, or 95.6 per cent., a vascular tubercle was discovered, most often in the pulmonary veins, but also in the thoracic duct, aorta, and other vessels. The author believes that these vascular tubercles of Weigert may be found in all cases of miliary tuberculosis which are carefully studied at autopsy, and explains the failure to localize this process in his 5 per cent. of negative cases principally by the difficulties of technique. The author agrees with Weigert in concluding that for the origin of the typical acute form of generalized miliary tuberculosis a localized tuberculous nodule in a vessel is necessary. It is conspicuous that the vascular tuberculosis arises only exceptionally by the extension of a tuberculous process from the surrounding tissue, but develops usually from the implantation upon the intima of the vessel of a few tubercle bacilli carried there by the blood stream. Occasionally foci of tuberculosis are found in several vessels. From these tubercle bacilli may be swept throughout the body. This fact possibly explains the occurrence of tubercles of different sizes in the same organ and in different organs.

Agglutination in Autoinfection, with Special Reference to Icterus.—Attention has been called by many observers to the fact that serum from certain jaundiced individuals possesses the power of agglutinating the typhoid bacillus.

LUDKE (*Deut. Arch. f. klin. Med.*, 1904, Bd. lxxxi. p. 34) reports the results of a series of observations and experiments bearing upon this point. He examined the blood from 32 cases of jaundice in adults due to various causes, and found that in 28 of this number the serum agglutinated the typhoid bacillus in dilutions of 1 : 20 or over. The agglutination was most constant and took place in the highest dilutions with the serum from cases of catarrhal jaundice. The agglutinating property of the serum withstood a temperature of 55° C. to 60° C. for half an hour, but was destroyed when the temperature was raised to 65° C. to 70° C for an equal length of time. The serum from 7 cases of icterus neonatorum gave no reaction with typhoid bacilli. Further studies showed that the serum from cases of nephritis and diabetes occasionally showed a mild reaction, while with cases of perityphlitis and chlorosis the reaction was frequently present, occurring in dilutions up to 1 : 60. In jaundice the serum agglutinated not only typhoid bacilli, but reacted as well toward bacillus paratyphosus, bacillus coli, bacillus lactis aërogenes, and the spirillum of cholera. Agglutination, however, was never as high or as well marked with these organisms as with bacillus typhosus. The above observations suggested that in jaundice the agglutinating power of the serum was not due to the presence of bile pigments in the blood, but was rather dependent upon a concomitant infection set up by some organism closely allied to bacillus typhosus. Further experiences substantiated this view. Typhoid bacilli were not agglutinated with bile alone, nor with blood mixed with bile. Neither was there any reaction with the serum from animals injected with bile. Taurocholic acid alone had no effect, but the serum from animals injected with this acid showed a slight and inconstant agglutinating property. The serum from animals jaundiced by means of injections of toluylendiamin and inhalations of arseniuretted

hydrogen showed no increase in the agglutinating power for typhoid bacilli; though with ether injections a slight increase was noticeable.

The author concludes that the serum agglutination of typhoid bacillus may take place under three different sets of conditions: 1. After typhoid infection. 2. Following infection by other organisms, as when agglutination takes place with the sera from certain cases of catarrhal jaundice, cholelithiasis, etc. 3. Through a disturbance in the normal relation of the components of the blood, as in certain blood diseases, icterus without infections, etc.

The Disappearance of Bacteria from the Circulating Blood.—The problem of latent bacterial infections has recently received some study, and the work of Tizzoni and Panichi has shown that animals immunized against the pneumococcus may harbor in the circulating blood living pneumococci after subsequent intravenous injections for weeks or even months. SCHWARZ (*Zeitschrift f. Heilkunde*, 1905, Bd. xxvi. p. 293) records some experiments upon the disappearance of typhoid bacilli from the circulating blood of guinea-pigs after intravenous injections of subminimal lethal doses of this organism. He found that the bacteria disappeared from the blood very slowly. After small doses typhoid bacilli could be cultivated from the blood of the animals six and sometimes eight days after injection, although the actual time required for the disappearance of the bacteria from the blood seemed to be dependent upon the amount of the culture injected. The spleen, bone-marrow, and lymph glands harbored living bacteria often in large numbers long after the cultures from the blood gave no growth. These organs almost always contained typhoid bacilli fourteen days after the primary injection, and in one case the bone-marrow was found to contain living bacilli one month after the intravenous inoculation of $\frac{1}{10}$ of an oese of typhoid culture. During the first few hours after injection the numbers of bacilli decrease rather rapidly in the blood and increase proportionately in the spleen. The result of these experiments, the author believes, does not uphold the view that actively bactericidal substances circulate in the blood. The destruction of the injected bacteria may not take place suddenly in the great vessels, but rather gradually in certain organs through the activity of the body cells.

In a paper upon "General Septicæmia," DUVAL and LEWIS (*Journal of Medical Research*, 1905, vol. xiii. p. 534) report among other cases one in which there was a so-called latent infection by bacillus mucosus capsulatus in man. This organism was obtained from the blood of the patient in pure culture a day after admission to the hospital; again after a week; and even in greater numbers, as demonstrated by plate cultures, the day of discharge. On discharge the patient had apparently recovered completely from his illness and looked perfectly well. Two weeks later he was at work.

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All communications should be addressed to—

DR. FRANCIS R. PACKARD, 1831 Chestnut Street, Philadelphia, U. S. A.

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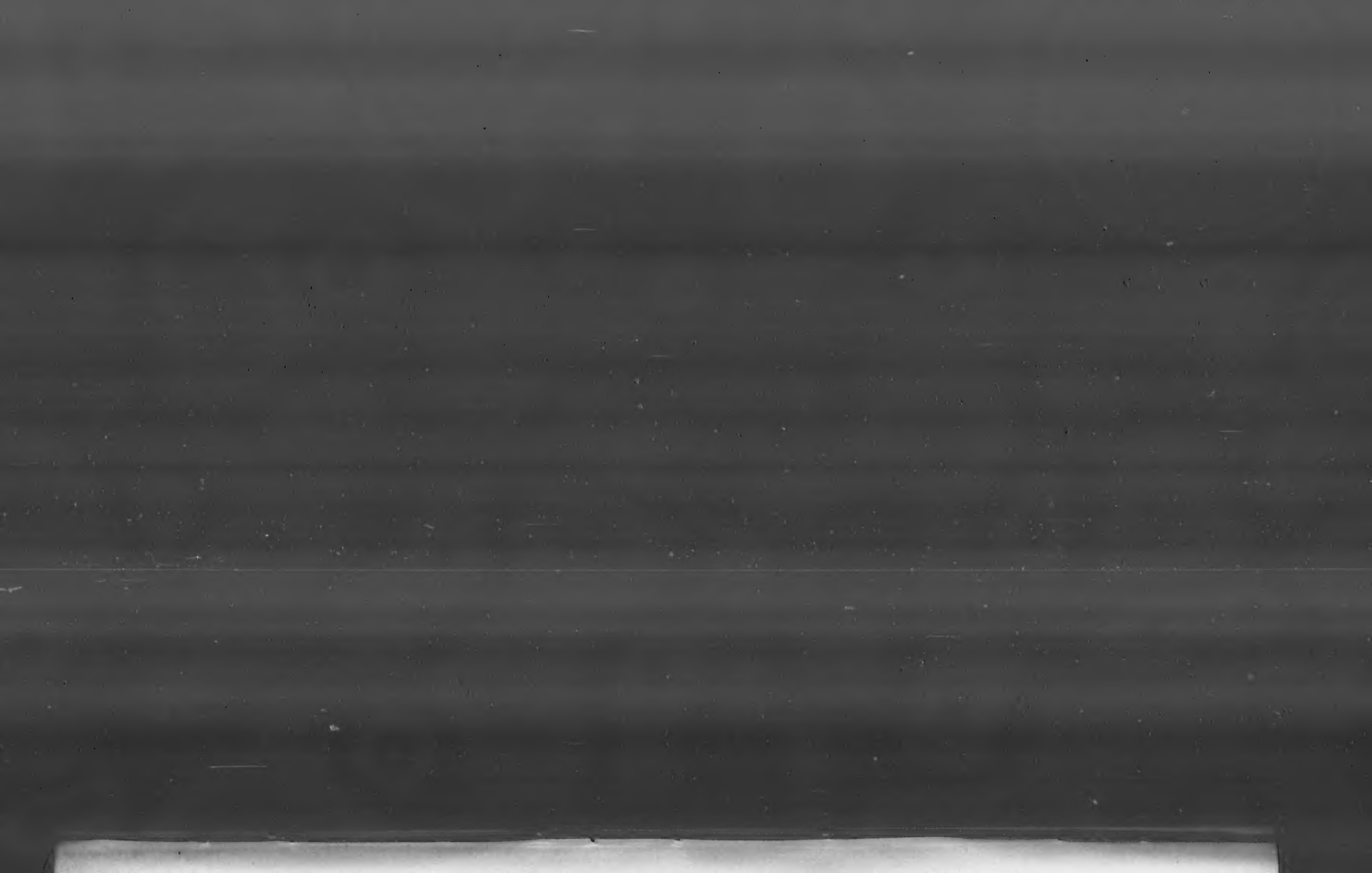

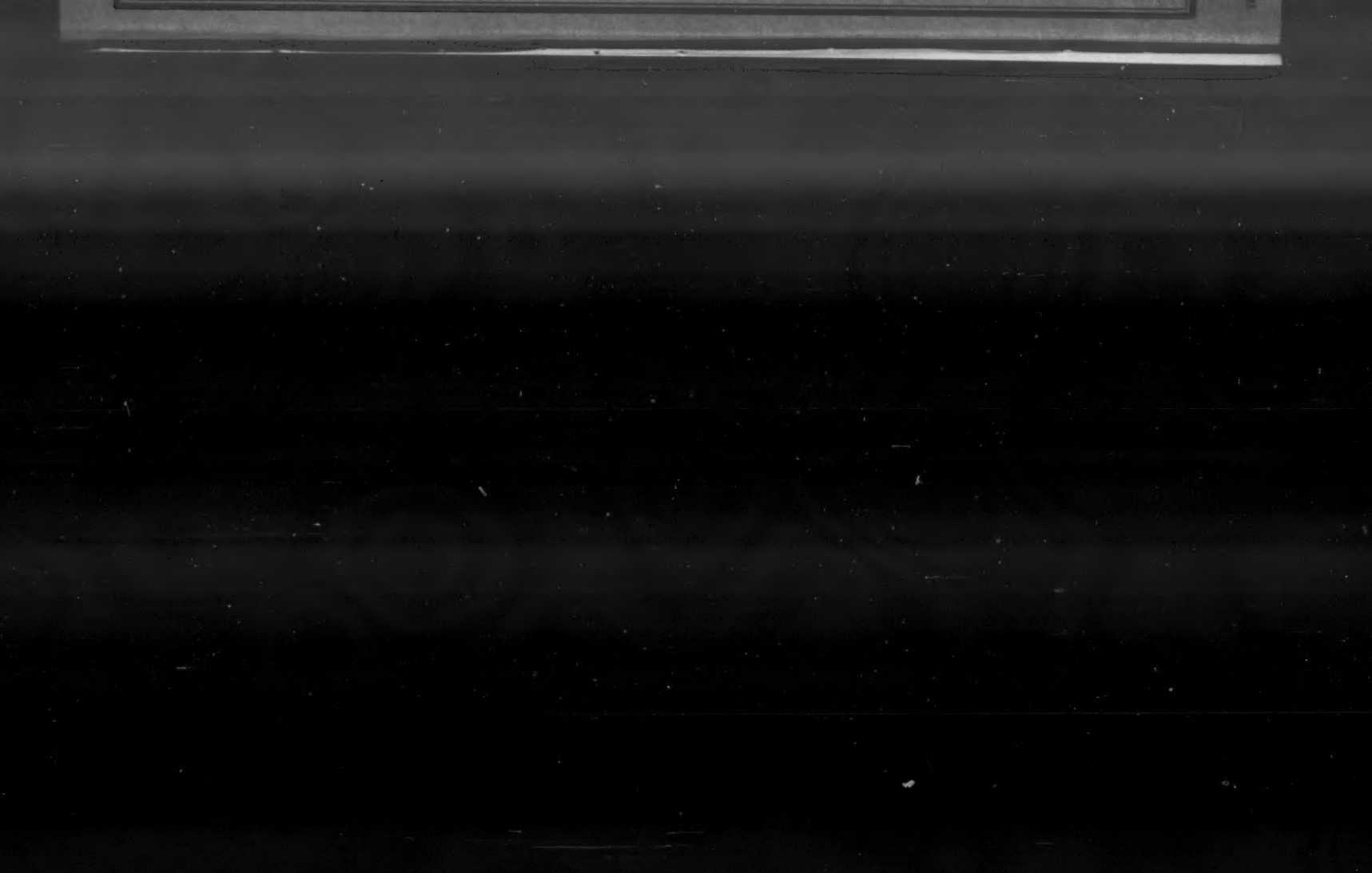

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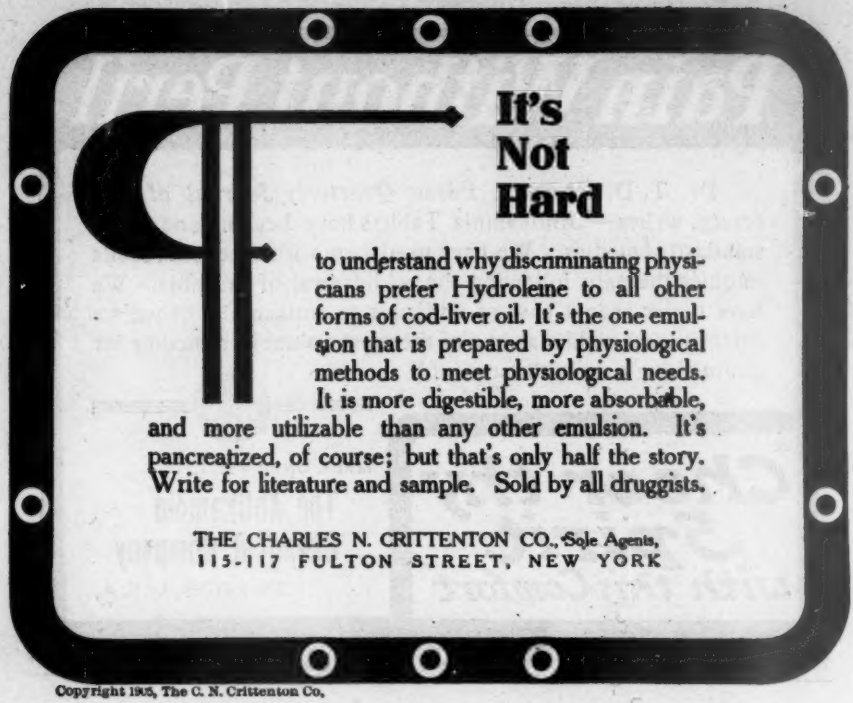
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